Rem. Inst. Med.
Society Library
12-27-1929

THE
BRITISH JOURNAL OF SURGERY

VOL. XIII. OCTOBER, 1925. No. 50.

EPONYMS.

BY SIR D'ARCY POWER, K.B.E., LONDON.

XVIII. BRYANT'S ILIO-FEMORAL TRIANGLE.

THE name of Mr. Thomas Bryant is associated with a pair of torsion forceps, a splint, and a surface-marking. The torsion forceps has gone into the limbo which sooner or later receives all surgical instruments. The splint is less used than it was. The diagnostic value of the ilio-femoral triangle remains. The first description of it appears in the course of a clinical lecture delivered at Guy's Hospital on December 16, 1875 (*Lancet*, 1876, i, 119), though attention seems to have been drawn to it at a meeting of the Royal Medico-Chirurgical Society on February 9, 1875.

Mr. Bryant introduced his subject with the following words: "The interest that is attached to the subject of injuries of the hip-joint, the difficulty that occasionally attends their diagnosis, and the injury that is too often inflicted upon a patient in the attempt to make out a difficult case, are some of the reasons that have induced me to bring before your notice on the present occasion a means of diagnosis in these cases that I have long employed and taught, although I may not have formulated it before the present year.

"I have described the means in this paper as the ilio-femoral triangle, and I have done so because the triangle is formed between the ilium and the femur. The lines which form it are readily made out and any shortening of the one which I have called the base, and to which I am about to draw your especial attention, can be easily detected.

"The triangle is formed as follows, and is a right-angled triangle. It is figured below (*Fig.* 120). One side of the triangle is represented by a line A B, drawn from the anterior superior spinous process of the ilium to the top of the trochanter major. The second, A C, is drawn from the anterior superior spinous process of the ilium directly downwards to the horizontal plane of the recumbent body. And the third, C B —which is the base of the triangle— is drawn at right angles to A C and falls upon the line A B, where it touches the great trochanter. It is to this line my observations refer. The line AB it will be seen corresponds in part to Nélaton's well-known line, which is

drawn from the anterior superior spinous process of the ilium to the most prominent part of the tuberosity of the ischium. This line in the normal position of the head of the femur, touches the upper border of the trochanter major in every position of the limb, and I believe that if this line is to be considered to be the test-line for dislocation of the head of the femur backwards—which I take it to be—I must claim the base of the triangle I have described (C B) to be the test-line for fracture or shortening of the neck.

"At any rate I can confidently assert, after repeated proofs, that whilst in a healthy subject these ilio-femoral triangles are exactly similar upon the two sides of the body, with equal sides and equal angles, I can with equal confidence assure you that in all cases of injury to the hip in which shortening of the neck of the thigh-bone exists, the amount of shortening can readily and accurately be made out on comparing the bases (C B) of the triangles of the two sides. That in impacted fracture of the neck of the thigh-bone, where on the sound side the base of the triangle will, in the adult, measure its average normal length of two and a half inches, on the affected or injured side it will measure from half an inch to more than one inch less. These

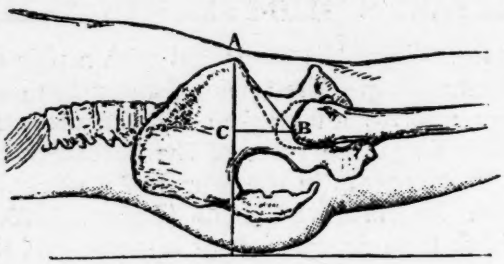
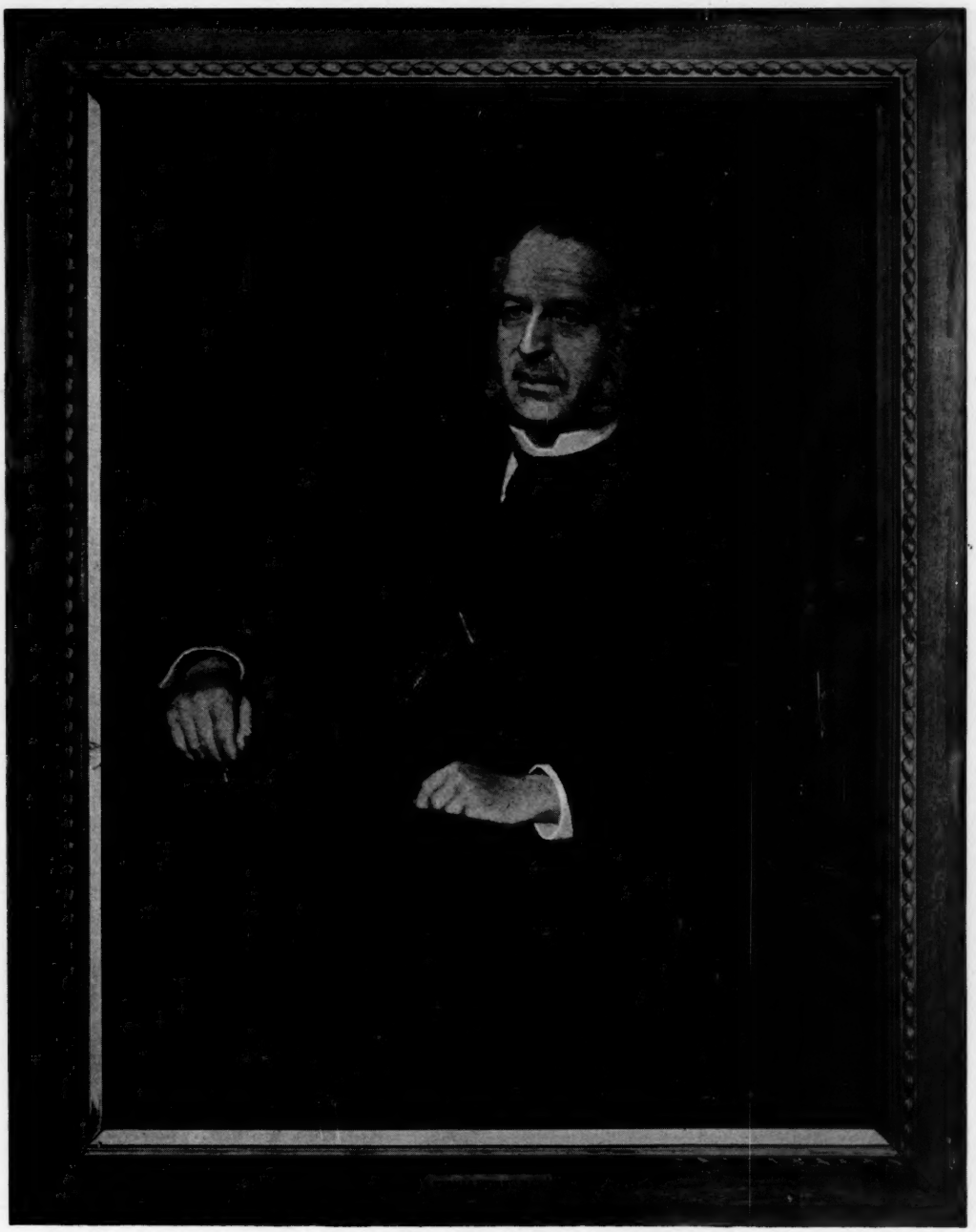


FIG. 120.—Bryant's triangle.
(*Figs.* 120 and 121 are facsimiles of the original illustrations in the *Lancet*.)

measurements being taken with the patient in the horizontal position, the pelvis straight, and the two femora parallel."

He then gives details of six cases of injury to the hip in which the ilio-femoral triangle had been useful in making a diagnosis, and adds that "in practice the line is easily made out and the test as to shortening of the neck of the femur readily applied, and with these facts before us the value of the means for diagnostic purposes can hardly be disputed. By means of this line the diagnosis of an impacted fracture of the neck of the thigh-bone can, as a rule, be made out with facility and certainty; and in a large number of obscure cases of injury to the hip the doubts and difficulties that were formerly experienced may be exchanged for the confidence of accurate knowledge. I do not mean, however, to say that by means of this test-line all obscure cases of injury to the hip-joint can be cleared up, for such an assertion would not be true; but I would wish you to believe what I have found to be the case—that by its use a large number of cases that would have been called obscure have ceased to be so. It is true there may be some shortening of this line in cases of fracture of the great trochanter, and it is likewise possible that there may be *no* shortening of the line in some examples of impacted fracture; but these cases are exceptional, and they in no way tend to diminish the diagnostic



UNIV. OF MICH.

value of the means I have to-day brought before your notice in the majority of cases of fracture of the neck of the thigh-bone, and in all cases in which shortening of the neck of the femur may be found. With these remarks I respectfully commend this test-line to your notice and adoption."

Mr. Bryant continues: "I think I shall be able to show that the opinion I have already expressed concerning the value of the test-line has been satisfactorily proved to be true by the experience of my dressers in the wards of this hospital; for I can tell you, and with much satisfaction, that during the last three years at least sixteen consecutive cases of fracture of the neck of the thigh-bone have been admitted into my wards, and that all these sixteen left with good union of the broken bone and useful limbs."

TORSION FORCEPS.

"When in his prime", says a writer in the *British Medical Journal*, "there was much discussion and experiment in relation to the question of hæmostasis without ligatures. Charrière in 1858 introduced his catch forceps with a lock and ring handles like scissors, devised both for dressings and for hæmostasis by torsion. Two or three years earlier Weber had invented an anti-ligature forceps, which, however, never came into wide employment. Koeberle, a pupil of Spencer Wells, made use of Charrière's forceps for forcipressure, maintained for several hours or days, in 1862, and continued the practice until 1867, when he removed the pressure forceps at the end of the operation or sooner, as is now the almost universal practice. Péan in 1867, and Wells about 1872, brought forcipressure into general use. Bryant's *Practice of Surgery* appeared in that year, and the author strongly advocated in it the method of torsion, figuring the instrument still known as Bryant's forceps. The instrument was thus made known two years before the publication of that which is usually described in maker's list as 'Wells' forceps.' In 1874, however, Wells' forceps were used as much or more for torsion as for forcipressure, though on the other hand we must remember that it was first made for Spencer Wells in 1872, the year that Bryant's textbook first appeared". Mr. Bryant stated in the fourth edition of his textbook that in 200 consecutive cases of amputation of the thigh, leg, arm, and forearm, in all of which the arteries had been twisted and not tied, there had been no case of secondary hæmorrhage, and this at a time when nearly every wound suppurated. In no fewer than 110 cases it was the femoral artery which had been twisted.

BRYANT'S SPLINT.

Bryant's splint (*Fig.* 121), described in the *Lancet*, 1880, i, 159, was intended to keep the legs and thighs quite parallel and to obviate the necessity for a perineal band. It was a modification of De Morgan's splint, and consisted of two long wooden splints interrupted from a point below the great trochanter to just above the crest of the ilium, the interruption being designed to avoid pressure upon the hip. One splint was applied to the outer side of each limb, and the two were connected below the feet and over the chest by sliding rods which could be fixed at an appropriate width. Extension was maintained

by an accumulator band, and counter-extension was obtained by the weight of the patient's body when the foot of the bed was raised three or four inches by blocks placed beneath the feet. The splint served a useful purpose, for it was introduced at a time when much thought was being given to the treatment of tuberculous disease of the hip by physiological rest.

Mr. Bryant's life history was told sympathetically by Mr. Golding Bird in the sixty-eighth volume of the *Guy's Hospital Reports*. He was born in 1828, the son of Thomas Egerton Bryant, who practised at Kennington and was surgeon to the Lambeth Infirmary. His father had been educated at the United Borough Hospitals, was interested in surgical pathology—as became a pupil of Sir Astley Cooper—and was President of the Medical Society of London in 1837. He sent his son to King's College School, apprenticed him to Mr. Thomas Olliver Duke, of Herleyford Place, his successor as Surgeon to the Lambeth Infirmary, and entered him in 1846 at his old school at Guy's Hospital five years after the death of Sir Astley Cooper. Thomas Bryant obtained the M.R.C.S. Eng. in 1849, and was elected a Fellow of the Royal

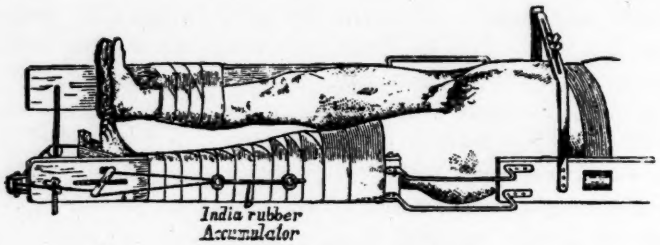


FIG. 121.—Bryant's splint.

College of Surgeons of England after examination in 1853. For some reason he never served as a demonstrator of anatomy as was then usual for those who aspired to the surgical staff of the hospital, but he was elected assistant surgeon in 1857, though he did not become full surgeon until 1871. He retired from the active staff in 1888 on reaching the age of 60, and having few distractions outside his profession he became surgeon to the Bolingbroke Hospital.

In addition to his hospital appointment he had a long and honourable connection with the Royal College of Surgeons, acting as Examiner, Member of Council, and President. In 1893 he was chosen to deliver the Hunterian Oration on the occasion of the hundredth anniversary of the death of John Hunter, the oration being given in the presence of H.R.H. The Prince of Wales, afterwards H.M. King Edward VII, and his son the Duke of York, afterwards H.M. King George V. In 1896 he was appointed Surgeon-Extraordinary to Queen Victoria, and later Surgeon in Ordinary to H.M. King Edward VII.

He published in 1872 a *Manual for the Practice of Surgery* which had a large sale in the United States as well as in this country. The book was essentially clinical, and was written in an easy style which made it especially acceptable to those who did not intend to practise surgery as a specialty. He also wrote an excellent clinical book on the *Diseases of the Breast*, consisting

of material drawn chiefly from his own experience. It appeared in England in 1887, and was published separately in New York in 1889.

He died on December 31, 1914, having married in 1862 Adelaide Louisa, daughter of Mr. Benjamin Waldrond, whom he survived three years and by whom he had four sons and three daughters.

Mr. Bryant, like his contemporary Sir William Savory, was unable to appreciate the great work which was being done by Joseph Lister. Bryant and Savory were both clinical surgeons without real scientific training. Both were wedded to the methods which they had practised for many years and by which they obtained better average results than some of their colleagues, partly owing to their greater operative skill, and partly by the attention which they bestowed on the after-treatment of the patients upon whom they had operated. Both, therefore, had attained the dangerous mental attitude of believing that surgery had attained to perfection.

Cheery, optimistic, and of pleasant manners, Bryant soon attained a very large surgical practice, driving about the town in a private hansom cab when he was very busy, in a one-horse brougham when there was less to do, and in a carriage and pair when business was slack. There were fewer operations for London surgeons, and no nursing homes for their patients, in the middle of the last century, and the professional work of a successful consulting surgeon lay within the compass of a horse drive, except for an occasional railway journey.

The portrait is copied from the oil painting by M. Hickson which hangs on the grand staircase at Guy's Hospital, and is a good likeness.

ON OSTEITIS DEFORMANS (PAGET'S DISEASE) AND ITS RELATION TO OSTEITIS FIBROSA AND OSTEOMALACIA.

By R. LAWFORD KNAGGS, London.

(Being a Hunterian Lecture delivered before the Royal College of Surgeons of England on February 11, 1925.)

Fifty years have passed since Sir James Paget, shortly after vacating the presidential chair of this College, read his celebrated paper upon the disease which I have chosen as the subject of this lecture. In the interval osteitis deformans has become an easily recognizable affection known to every practitioner, and many interesting examples have been recorded. The time therefore is suitable for a review of the subject, that we may note the additional knowledge that has accumulated, and try to estimate what is the relation of this peculiar condition to some other bone affections.

Osteitis deformans is the name suggested by Paget, and now applied by general consent to a very chronic disease of an inflammatory nature, occurring in middle-aged or elderly people, in which the normal osseous structure of the skeleton is removed, and fresh bone, formed on a different plan and in a larger mould, takes its place.

As an acknowledged separate affection osteitis deformans dates from Sir James Paget's communication to the Royal Medico-Chirurgical Society in 1876. In 1869 Wilks had reported a remarkable case under the title, " A case of osteoporosis or spongy hypertrophy of the bones ", and Paget supported his own case with that of Wilks and others of a similar nature that were on record, and contended that their very definite and peculiar characters justified the recognition of a new disease. Paget was inclined to believe that the disease was of quite recent origin; but the existence of various old museum specimens, now recognized as examples of osteitis deformans, show that it had attracted attention long before modern times. Indeed, Paget, when he wrote his Bradshaw lecture,[1] must have overlooked a splendid example which it is believed that he himself had described in the Museum Catalogue. This is a skull (R.C.S. Museum, No. 693) which was dug up in Stepney Parish Churchyard, and was included in John Hunter's original collection.

In the present review the different features of the disease will be studied under the following heads: (1) *The clinical aspects;* (2) *The bone changes, macro- and microscopic;* (3) *The complications;* (4) *The pathogenesis;* (5) *The correlation of osteitis fibrosa, osteitis deformans, and osteomalacia;* (6) *Causes that may determine the onset of the disease.*

1. THE CLINICAL ASPECTS.

There are two characteristic types. In one the bone changes affect so many bones that the disease may be spoken of as 'generalized'. In the other they are limited to a single bone—at least for many years.

As a rule, in the *general affection* the bones are attacked in a definite sequence. Though atypical cases occasionally occur, the usual form is that described by Paget in the following epitome taken from his paper :—

The disease " begins in middle life or later, is very slow in progress, may continue for many years without influence on the general health, and may give no other trouble than those which are due to the changes in shape, size, and direction of the diseased bones. Even when the skull is hugely thickened and all its bones exceedingly altered in structure, the mind remains unaffected. The disease affects most frequently the long bones of the lower extremity and the skull, and is usually symmetrical. The bones enlarge and soften, and those bearing weight yield and become unnaturally curved and misshapen. The spine, whether by yielding to the weight of the overgrown skull, or by change in its own structures, may sink and seem to shorten, with greatly increased dorsal and lumbar curves ; the pelvis may become wide ; the neck of the femur may become nearly horizontal, but the limbs, however misshapen, remain strong and fit to support the trunk.

" In its earlier periods, and sometimes through all its course, the disease is attended with pains in the affected bones, pains widely various in severity, and variously described as rheumatic, gouty, or neuralgic, not especially nocturnal or periodical. It is not attended with fever. No characteristic conditions of urine or fæces have been found in it. It is not associated with syphilis, or any other known constitutional disease unless it be cancer. In three out of five well-marked cases, that I have seen or read of, cancer appeared late in life ; a remarkable proportion, possibly not more than might have occurred in accidental circumstances, yet suggesting careful inquiry."

The impressive clinical accounts of their cases left to us by Paget and Wilks are not of historical value only, but are interesting reading for those who can only form some appreciation of those great teachers from their writings.

Sir James Paget's Case.[2]*—A healthy man of good family history began to be subject to aching pains in the thighs and legs after exercise at the age of 46 (1854), and in the following year his left shin was noticed to be misshapen. In 1856 the lower half of the left tibia was broad, nodular, and uneven, and there were similar changes in the lower half of the left femur. There was no tenderness, and the limb was occasionally, but never severely, painful. In 1859 the tibia had increased and showed a well-marked anterior curve, and as the fibula remained normal it suggested an increase in length. The femur also was enlarged, and arched forwards and outwards. The left lower limb was $\frac{1}{4}$ in. shorter than the right, the left side of the pelvis was affected, and his hat had become too tight. Though the left lower limb was clumsy the patient led the active life of a country gentleman. (*Fig.* 122.)

During the next seventeen years the disease progressed uniformly and slowly. The left femur and tibia became heavier and more curved ; the right limb followed till it acquired the same size and shape. The knees became gradually bent, and lost much of their natural range of movement, and the skull gradually grew larger, till, in 1876, the circumference of $27\frac{1}{2}$ in. was 5 in. more than in 1844, though the head still retained its shape and intellectual appearance. The spine developed a

---

* Illustrations of this case are also given in Sir D'Arcy Power's *Eponym* " Sir James Paget " in the BRITISH JOURNAL OF SURGERY, 1922, October, p. 161.

marked posterior kyphotic curve in the cervical and upper dorsal regions, and an anterior curve of the lower dorsal and lumbar vertebræ. Its length decreased, and his height sank from 6 ft. 1 in. to 5 ft. 9 in. The chest, owing to lateral flattening, became narrow, while its antero-posterior depth was increased. The posture was striking and simian. The head was advanced and lowered so that the neck was very short, and the chin more than 1 in. lower than the top of the sternum.

The short narrow chest suddenly widened into a much shorter and broad abdomen, and the pelvis was wide and low. The arms appeared unnaturally long, the hands hanging low down by the thighs and in front of them.

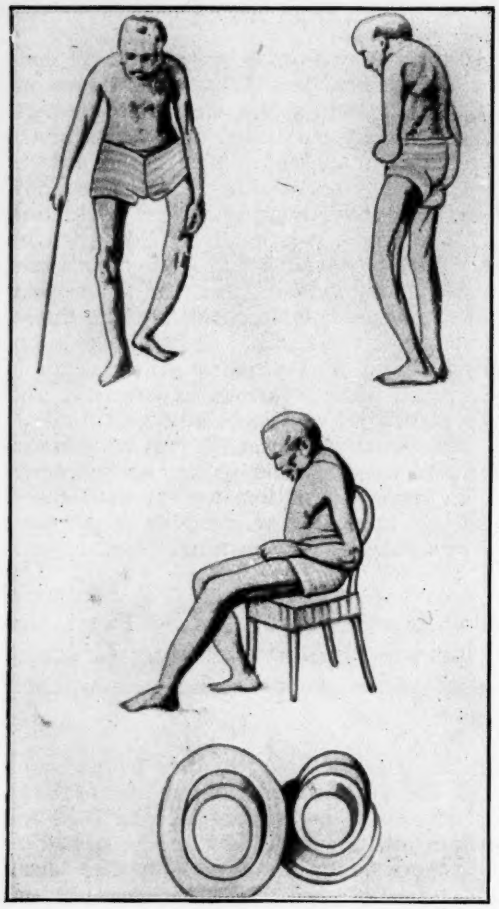


FIG. 122.—Reproduced from Paget's original paper (Gaenslen).

During the last three or four years of life the increase in the limbs and head was imperceptible. There was no disturbance of the general health, and the upper limbs remained perfect until in January, 1876, a swelling of the upper third of the left radius appeared and grew rapidly. The patient gradually failed and emaciated, and died on March 24 with pleural effusion due to metastatic growths in the right pleura, and nodules of growth in the vault of the skull. Except for the primary growth in the left radius the rest of the bone seemed quite healthy.

Dr. Wilks' Case.[3]—A man, aged 60 at the time of his death, had sought advice fourteen years before for pains in his legs. His tibiæ soon became enlarged, and after two years it was evident that all the bones in his body were increasing in size. The humerus, clavicle, and cranium were all involved, and subsequently the ribs.

A year before his death his health began to suffer from the implication of the thorax, and from this time it was apparent that his days were numbered. "At this period he was accustomed to sit in his chair with his head bent forward and chin resting on his breast, his arms and legs almost useless, and his breathing very difficult from want of expansion of the chest."

"When stripped and assisted to stand in the erect position his figure resembled much more that of an ape than of a man. He had become shorter in stature, his legs were somewhat bent, his arms fell in front of him, his head dropped forwards, his chest was narrowed, pelvis contracted" (described by Dr. Goodhart—p.m.—as of the rickety type) "and belly protuberant, and thus all characteristics of a manly figure lost."

"After this the chest became more contracted, and at last quite fixed, so that the respiratory process was effected entirely by the diaphragm. Breathing became painfully difficult and dropsy of the legs ensued . . . the breathing became more difficult until at last the respiratory apparatus altogether stopped."

A cauliflower growth (endothelioma of the arachnoid) was growing from the inner surface of the dura mater, and pressing into but not involving the brain.

In some cases the incidence of the disease does not follow the usual course. Clutton[4] recorded the case of a woman, in whom, though the usual bones were affected, the disease reached its height in the upper extremities; and Joseph Griffiths[5] has described a skeleton in the Cambridge Museum which had the same peculiarities.

Wherry[6] amputated a leg for sarcoma of the tibia in a man, age 56, in whom the skull and vertebral column were the parts chiefly affected.

The long bones were not obviously diseased in Goodhart's case[7] of the old post-boy, but the skull was remarkably affected, and the clavicle, 1st rib, spine, and pelvis were involved.

Possibly Paget's doubt as to Rullier's case[8] was due to the fact that the bones of the limbs were normal and appeared small and disproportioned when compared with the other parts.

Lastly, one of J. R. Lunn's cases[9] (*Case* 3) had ankylosis of both hips and stood with crossed legs. This was almost certainly due to complications and not to osteitis deformans. The joint troubles were unusually marked.

The type in which *one bone only* is affected is more frequent than published cases would suggest. Many surgeons believe that in these cases trauma is more often the exciting cause than in the generalized type. A history of a contusion or a fracture antecedent to the onset of the disease is common, but it is not always to be obtained, and as the interval between the injury and the commencing deformity may be considerable the point is a difficult one to settle. The best known instance of this limitation of the disease is that recorded by Bowlby[10]:—

A cabman, age 64, died in St. Bartholomew's Hospital from fractured skull and cerebral hæmorrhage. His left femur presented the usual signs of the disease. It was curved in an outward and forward direction, and very flattened antero-posteriorly. Its circumference at its thickest part was $6\frac{1}{4}$ in. Its surface was rough and uneven, and the neck was at right angles to the shaft. It was the only bone affected, and had become curved during the last ten years of life. A few months before death the shortening amounted to $2\frac{1}{2}$ in. (*Figs.* 131, 131A)

The following case was associated with trauma and complicated with ulcer and necrosis, conditions which will be subsequently considered:—

J. R., age 63, broke his right leg thirty-four years before admission to the Leeds General Infirmary. For a good many years following the fracture walking had caused great pain, and for the last twenty years the leg had been slowly bending. He had had to give up his work nine years ago, and after that the leg became swollen, and an ulcer formed which never healed. The limb was amputated by Mr. Littlewood. The tibia was the only bone affected.

It is the bone changes that constitute the important and characteristic feature of osteitis deformans. One symptom—pain—is directly connected with them.

Pain in the bones is usually marked long before any alteration can be detected in them. It continues during the progress of the bone changes and varies in intensity. In some cases it is not present at all, or is insufficient to attract attention. Joncheray has distinguished a painful and a painless

variety, and believes that the osseous lesions develop more rapidly in the former. Hurwitz has described two cases of the painless form (*Cases* 2 and 4) in which the disease developed marked features unsuspected by the patients, who came under observation for the results of cardiac and vascular trouble and not for any condition arising from the bone disease.

The period of life in which the disease begins is a point of considerable importance. It is rare for osteitis deformans to start before the age of 40, but earlier cases have been recorded. In Morris's case the symptoms began at 30, and in Paget's *Case* 7, a woman, as early as 28.[11] On the other hand, Packard states that out of 41 males and 24 females, the youngest reported was Watson's at 39. One or two cases have been met with below the age of 20, but such cases should be looked upon with suspicion, and only accepted with caution. They fall within the period of life when osteitis fibrosa develops, and there has been much confusion between the two diseases. I recently examined a section from a clavicle removed from a girl of 19 which had long been regarded as an instance of osteitis deformans. The microscopic appearances were those of osteitis fibrosa (Leeds Medical School Museum, old No. A119b (*see* p. 231), new No. A814).

On the other hand, Mr. P. B. Roth recently reported to the Orthopædic Section of the Royal Society of Medicine the case of a man of 30 whose right tibia had been growing bigger since the age of 18. The skiagram, shown at the meeting, was typical of osteitis deformans. The tibia was the only bone affected.

2. THE BONE CHANGES.

Enlargement and softening characterize the bones which are attacked by osteitis deformans. The long bones are not only greatly thickened, their circumference and sectional area being much enlarged, but they are also elongated and unduly curved. The alteration in the normal curves, not only of the bones of the lower extremities but of the spine, is due to the superincumbent weight acting upon bone softened and rarefied by the disease. In the upper extremities, sometimes, different but not very dissimilar causes are at work. In some instances bending is produced by the elongation of a bone attached at both ends to another bone which has not been affected. This happens in the forearm and the leg. Notwithstanding the elongation of the long bones, a decrease in height is a constant result of osteitis deformans. It may vary from a few to $13\frac{3}{4}$ inches (Hurwitz,[12] *Case* 5), and depends chiefly upon the curving of the spine and of the bones of the lower extremities.

THE SKULL.

It is exceptional for the skull not to be greatly enlarged. The increase in size is at first associated with great vascularity, but this slowly wanes as sclerosis develops. Three typical stages can be recognized.

1. **The Vascular Stage.**—In this the bone is of a marked red colour due to the permeation of the new porous bone from side to side by a very vascular connective-tissue marrow. It was present in the cranium of a woman, age 65, who had suffered constant pain in the head—often severe—for fourteen years. Its circumference had increased nearly an inch (to $25\frac{7}{8}$ in.) during the

FIG. 123.—The vault of the skull of Dr. Hann's case. Miss Wright has given a very good representation of the present colour of the skull. When fresh the red colour was more pronounced. (*No. A 26n, Leeds Medical School Museum.*)

UNIV.

four years she was under observation. The vault is still of a brick-red colour, testifying to its great vascularity; and owing to its softness it was removed with great ease. Condensation on the inner and outer surfaces is in an early stage, but not differentiated in colour from the open porous tissue which constitutes the bulk of the calvarium. The sutures are not obliterated and the frontal sinuses persist. Microscopically the vascularity was very evident. (*Fig.* 123). (Leeds Medical School Museum, No. A26n.)*

2. **The Stage of Advancing Sclerosis.**—Many museum specimens illustrate this stage. The skull of Paget's case is a good example (R.C.S. Museum, No. 1239) (*Fig.* 124). In it the thickness of the vault in every part is four times the normal, and the sutures of the vertex are obliterated. Its outer surface is smooth, but perforated by multitudinous minute apertures. It is the surface of very finely cancellated porous bone. The inner surface is similarly

FIG. 124.—Sagittal section through the cranial vault of Paget's case. Note the sclerosed condition of the inner part of the section and the islet of condensed bone on the right. (*No.* 1239, *R.C.S. Museum.*)

but less obviously porous. It is deeply grooved for meningeal vessels, and perforated by numerous vascular foramina. The general character of the interior of the bones, whether of the vault or base, is a finely porous or reticulate condition differing in degree and uniformity in different parts. A section through the vault shows the bone contiguous to the inner surface to be very condensed for a thickness of $\frac{1}{4}$ to $\frac{1}{2}$ in., but it is still finely porous. (Paget described it as " hard white-looking bone, dense like limestone ".) The rest of the section shows various degrees of porous, cavernous, or cancellous tissue whose spaces were filled with soft reddish substance, whilst the outer surface is bounded by a thin line of condensed porous bone of the thickness of paper.

3. **The Stage of Complete Diffuse Sclerosis.**—This is exemplified by the cranial vault of Dr. Goodhart's case (R.C.S. Museum, No. 705.1, Gen. Path.

* The case, which is of much interest, was recorded by Mr. R. G. Hann (*Brit. Med. Jour.*, 1910, i, 135). The patient died with cerebral symptoms, but no gross lesion was found in the brain. The botryoidal elevations on the inner surface of the vault are not commonly of such a size.

Sec.) (*Fig.* 125). The sclerosis has advanced across the diploic zone and invaded in an irregular and patchy manner the finely porous tissue which may be considered to represent a thickened external table. In the vertex, but not at the sides, the cancellous diploic area is still recognizable where it is not crossed by sclerosed tracts, but it is very narrow. The specimen presents an ivory-like appearance with a white and somewhat polished exterior (*see also* No. 1241Bk, R.C.S. Museum—another example). On the internal surface a small opening leads into a cavity big enough to hold a damson, and occupying almost the whole thickness of the skull.

In skulls that illustrate the last two stages, *sharply defined islets of ivory-like bone* may frequently be seen on the face of the sections isolated in a

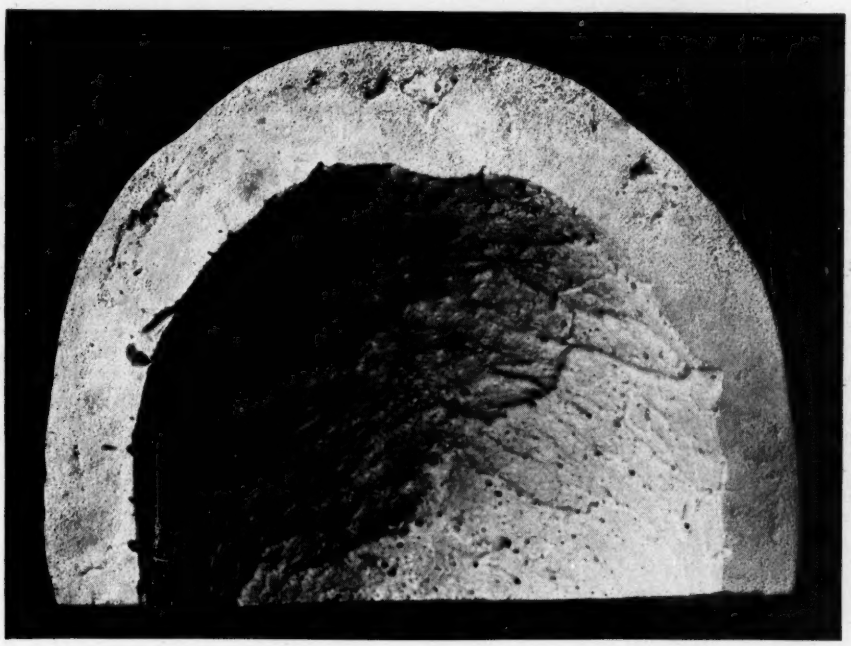


FIG. 125.—Showing complete sclerosis of the cranial vault. There is an islet of condensed bone near the top of the picture, which looks as if it were in process of separation. Goodhart's case. (*No.* 705.1, *R.C.S. Museum, Gen. Path. Sect.*)

cancellous area or surrounded by a thin line of porous tissue in a sclerosed part. Some are defined by what is suspiciously like a line of demarcation, which suggests that they may eventually become sequestra. Possibly the cavity in the vault of Goodhart's case may at one time have contained a sequestrum which became absorbed during the long duration of the disease.

THE FRONTAL SINUSES are usually found open when the section through the skull passes across them. They tend to become smaller or even obliterated in advanced cases, but this tendency is not so marked as in both varieties of leontiasis.

THE CRANIAL CAVITY is not clearly diminished in these hypertrophied skulls, the increase in the thickness of the bone taking place almost entirely outwards.[13] The earlier sclerosis of the inner portion of the vault may be

explained by the compression of its interstitial substance owing to the resistance of the cranial contents to the inward expansion of the enlarging bone.

THE BASE OF THE SKULL may appear quite normal in some cases, but in a fair proportion it is obviously involved. Then the bones appear swollen, the grooves for the meningeal vessels are deep and sharply margined, and the pituitary fossa may be altered. The various foramina are not seriously contracted, though the regularity of their margins may be impaired. This is most noticeable in the foramen magnum (R.C.S. Museum, No. 1241 Bk). Wyllie,[14] commenting on this narrowing of the neural foramina and the rarity with which the cranial nerves show signs of compression, records two cases in which optic atrophy very possibly depended upon compression of the nerves at the optic foramina. On the other hand, the vascular foramina have occasionally been found enlarged, presumably from the pressure exerted upon the softened margins by the pulsation of the transmitted vessels.

The anterior fossa in some instances presents a curious appearance. A deep V-shaped depression with shelving sides and its apex at the cribriform plate is produced by the great thickening spreading to the orbital plates from the frontal bone.

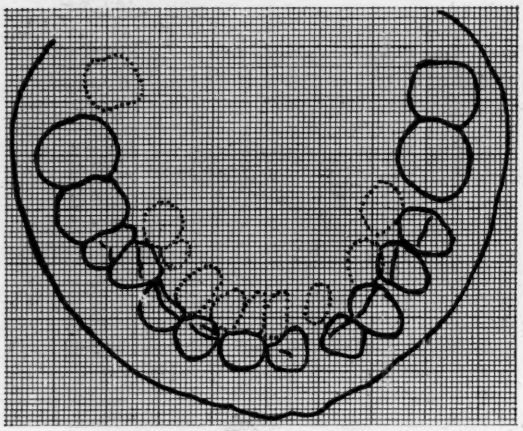


FIG. 126.—Diagram plotted from casts of upper and lower jaws from a case of osteitis deformans, showing the enlargement produced in the alveolar arch of the upper jaw by the disease, and the position of the alveolar arch of the lower jaw within it. (*By the kindness of Sir Frank Colyer.*)

The softened cranial bones will give way to pressure like the long bones, and a suggestive asymmetry may result. In one skull, probably as a result of the position in which the head was rested, the posterior fossa on the right side was narrowed and elongated, and the internal occipital crest deviated to the left (St. Thomas's Hospital Museum, No. 422). In another the left posterior fossa was narrowed, whilst the parts about the foramen magnum appeared pushed up and produced a hollow on the under surface of the base (Univ. Coll. Hosp. Museum, No. 652, Bone 64H). It has been pointed out that those parts of the skull formed from membrane are more conspicuously affected than those formed from cartilage, but the relative proportions of compact and cancellous tissue are probably more important than the mode of origin. It is easy to realize that the petrous bone will resist absorption and expansion much more than bones with a thin cortex and a considerable cancellous interior.*

THE FACIAL BONES are commonly thought to escape, and probably a

---

* In the *Journal of Laryngology and Otology*, 1923, July, xxxviii, 344, G. J. Jenkins discusses deafness in connection with osteitis deformans. Nine cases with obvious affection of the skull bones suffered from deafness in some degree. He came to the conclusion that deafness is not obvious until the skull bones are affected.

slight involvement often evades notice. Sometimes, however, they are markedly affected (Univ. Coll. Hosp. Museum, No. 652, Bone 64H.)

In the case of an edentulous man who was so deaf that no history could be obtained from him, the alveolar processes of the superior maxillæ were greatly thickened and rounded, and the dental arch so much enlarged that the unaffected alveolar margin of the lower jaw fitted completely and easily within it, like the rim of a box inside its lid (*Fig.* 126).*

FIG. 127.—Skiagram of a skull of a man, age 54. The change in the skull was noticed twenty years before. (*From a case of Mr. C. P. G. Wakeley's.*)

* Mr. J. G. Turner showed to me at the Royal Dental Hospital a retired policeman, age 62, who had first noticed the disease in the right tibia twenty years before. Both tibiæ, the lower half of the right humerus, and the right clavicle were affected, and the size of the head had been increasing steadily (circumference 26 in.). The face bones were all enlarged —both malars, the two maxillæ, and the mandible. The enlargement of the maxillæ was most marked, and when the edentulous jaws were closed the mandibular arch lay completely within that of the maxillæ. In addition to the general enlargement of these bones there was a circumscribed local enlargement of the molar region of the alveolus of the left maxilla. When the patient came under Mr. Turner's care both jaws were full of very foul teeth, and there was much pyorrhœa. The dental trouble must have existed many years, and probably dated back as far as the commencement of the bone disease. All the septic teeth, to which large masses of granulation tissue were adherent, were cleared out, and portions of bone removed from all round the upper alveolus, including the local enlargement, to lessen the deformity. Not only was the jaw condition improved by this, but so also were the tibiæ, for the skin over these bones had been œdematous and inflamed and the bone tender, and this speedily cleared up.

In a man of 65 under the care of Sir Gordon Watson both upper jaws were considerably enlarged. The enlargement was general, and more marked on the left side. The body of the lower jaw was thickened. There was some dental trouble, but it was not severe. In both cases the jaw trouble was part of a generalized condition.

Cases in which the jaw enlargement would appear to have been only a local phenomenon are found in the literature of osteitis deformans. They are more likely to have been cases of osteitis fibrosa and probably dependent on dental irritation.

THE SPINE.

The curving has been described in Sir James Paget's epitome.* It is not infrequently associated with traces of 'lipping' of the bodies, with synostosis of their articular surfaces, and ankylosis of the dorsal spine—conditions apt to be readily dismissed as osteo-arthritic, but in which pressure, compensation, and senile changes in the discs undoubtedly play their part. Thickening, rarefaction, and softening of the various parts of the vertebræ take place, and occasionally one or more vertebræ may collapse and become deformed (R.C.S. Museum, No. 1241 Bf. 1241Bk: St. Bartholomew's Hospital Museum, No. 74Ci). Dr. Goodhart found a deposit of new soft bone all down the front of the bodies in the spine of the old post-boy, and in a skeleton in St. Thomas's Hospital Museum (No. 417) the bony deposit on the spines, articular and transverse processes, and also on the crests and dorsal surfaces of the ilia, approximates in its characters to myositis ossificans.

FIG. 128.—Section through a lumbar vertebra of a case of osteitis deformans showing: (*a*) Diminution and alteration in shape of the spinal canal by the enlarging body and neural arch; (*b*) The projection into its lumen of bony outgrowths from the arch; and (*c*) The formation of a lip around the articular edge, probably the result of pressure upon the softened bone. (*College Stores, R.C.S. Museum.*)

But a change that is little known, yet of great importance, is the diminished calibre of the spinal canal which is brought about by the enlargement of the bodies and the bone composing the vertebral arches (*Fig.* 128). This may take place to such an extent that the cord and its membranes no longer lie loosely in the perithecal space, but come to fill the whole sectional area of the canal, and may even

* I am indebted to Mr. C. P. G. Wakeley for an account of a man, age 54, in whom the history of the disease dated back twenty years. He sought advice for an abdominal swelling, which proved to be caused by the liver pushed forwards by a very pronounced anterior arching of the lumbar spine. (*Fig.* 127 shows the skull in this case.)

be subjected to compression with resulting paraplegia. In such cases additional localized pressure points may result from the formation of small osseous excrescences springing from the posterior surfaces of the bodies and other parts of the wall of the canal (Greenfield).

Two cases of osteitis deformans in which compression of the cord with paraplegia was brought about in this way have been put on record by Dr. W. G. Wyllie from the National Hospital for the Paralysed and Epileptic, Queen Square.

In one, a man of 55, with marked changes in the skull, spine, and one tibia, suffered from increasing weakness and sensory disturbances in both legs, with vesical and rectal inconvenience. Mr. Percy Sargent performed laminectomy of the 2nd to the 4th dorsal vertebral arches. The bone was thickened and soft, and cut easily with the forceps. The perithecal space was absent, and the inner surface of the laminæ lay in close contact with the dura. Pulsation, which was at first feeble, improved as decompression was completed. The effect of the operation upon the symptoms was satisfactory. Sphincter power was regained, and the patient became able to walk much better.[15]

The other was a man of 63 who was admitted with complete spastic paraplegia which had been coming on gradually for two years. During an exploratory operation very similar conditions to those described in the preceding case were disclosed. At a subsequent post-mortem the spinal canal was found narrowed so that the dura mater was everywhere in contact with the thickened bone and also abnormally adherent to the arches all the way round. The bone disease appeared limited to the spine, but the condition of the long bones and the skull could not be investigated. It was in this case that Dr. Greenfield found that the cerebrospinal fluid, of which only a small quantity was obtained by lumbar puncture, was of a yellow colour and coagulated to a solid mass in the test-tube on standing (Froin's syndrome).[16]

THE LONG BONES.

To appreciate fully a description of the macroscopic appearances of the long bones it should be realized that the morbid process consists in a complete or almost complete removal of the original osseous tissue and the substitution for it of a cancellous bone of a finely porous character. The piecemeal removal of the former, and the formation of the latter, are brought about by an active young connective tissue* which permeates the trabecular framework of the bone from the fat medulla in the central canal (which often is only superficially involved) to the under surface of the periosteum, with which it blends.

This young connective tissue speedily shows that it has osteogenic properties. As the original bone disappears, new bone-formation begins in the osteogenic tissue which takes its place. The two processes—absorption and

* Though osteoclasts share in the removal of the original bone, as they certainly do in moulding the newly-formed bone, it is evident that the extensive destruction is out of all proportion to the number of osteoclasts present.

ossification—go on simultaneously, but the proliferating soft tissue forms first and slowly effects the expansion of the periosteal envelope during absorption, whilst the formation of new bone progresses more gradually. Thus soft and vascular tissue predominates in the diseased bones in the earlier periods of the disease.

Consequent upon these changes there ensues an excentric enlargement and

FIG. 129.—The upper half of a femur from Paget's case, showing its roughened and nodular surface. (*No.* 1240, *R.C.S. Museum.*)

FIG. 130.—This specimen may represent the stage of the disease which has been described in the text as the ' vascular stage ' ; but it is possible that the peculiar appearance may be due in part to atrophy from old age and disuse, and that the soft parts, instead of vascular connective tissue, may have been fatty. From a woman, age 73, who had been bedridden fifteen years and in whom the curvature of the tibia had been in progress thirty years. The head and right femur were also affected. (*Dr. J. R. Lunn's case. No.* 1241*Bn, R.C.S. Museum.*)

elongation of the bones, and a degree of softening, owing to the temporary inadequacy of the new bone-formation, which predisposes them to bend slowly under the influence of such forces as may be continuously or often in action. It is the bone, as distinct from the periosteum, that is involved in this process, and though the periosteum plays a part, it is not the subject of a true periostitis as that is generally understood. The periosteum limits the active tissue, shares in its nutrition, and no doubt assists in its superficial

development: not by the laying down of superficial laminæ, but rather by stimulating bone-production in the adjacent osteogenic tissue. The time arrives, however, when the ossification becomes more vigorous than absorption; the soft osteogenic tissue becomes largely turned into bone; and in the last stage the bones become dense, hard, heavy, and apparently strong.

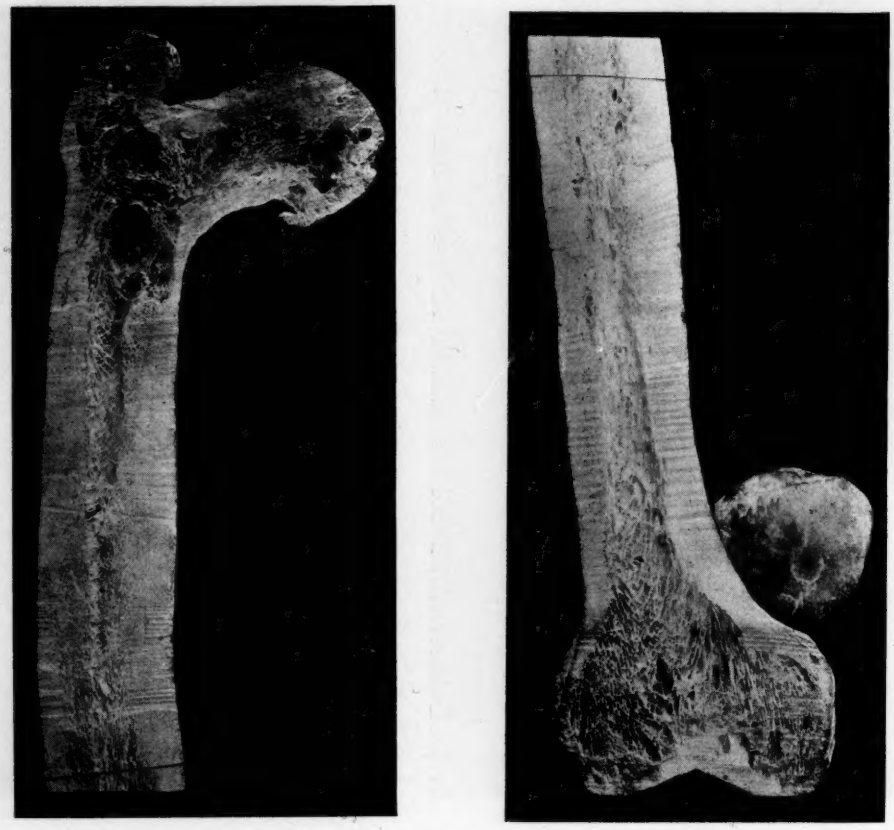
The bone changes affect both the external and internal appearances. Paget, describing the long bones and their *normal* periosteum in his case, wrote: "The outer surface of the walls of the bones was irregularly and finely nodular as with external deposits or outgrowths of bone, deeply grooved with

FIGS. 131, 131A.—Section through the femur of Bowlby's case—stage of advancing sclerosis. (*No. 1241Ba, R.C.S. Museum.*)

channels for the larger periosteal blood-vessels, finely but visibly perforated in every part for the transmission of the enlarged small vessels. Everything seemed to indicate a greatly increased quantity of blood in the vessels of the bone" (No. 1240, R.C.S. Museum, Paget's case) (*Fig.* 129). This irregular roughened surface of the long bones is very characteristic of the disease, and it will be noticed that Paget recognized that the irregularities might arise *from* the bone and not be laid down upon it.

The condition of the interior varies considerably, and, as in the skull, different stages may be distinguished. Thus *in some specimens* (macerated)

the interior of the bone shows a very open arrangement of trabeculæ with irregular spaces between them, which were no doubt occupied by vascular connective-tissue marrow of a deep-red colour. The original compact bone has disappeared and a sclerosed outer layer of porous bone of no great thickness is present (Tibia, No. 1241Bn, R.C.S. Museum) (*Fig.* 130). *In others* the shaft of the bone is composed of thick walls of condensed bone enclosing a central cavity, much elongated and often irregularly enlarged. Its boundaries may be very unevenly sclerosed, and exhibit patches of rarefaction and many open spaces having a longitudinal direction as if separating vertical lamellæ. In



FIGS. 132, 132A.—Section through the femur of Paget's case. Stage of complete sclerosis. Owing to the marked anterior curvature of the bone, the section has passed close to the periphery of the central cavity in the middle portion. (*No.* 1240, *R.C.S. Museum.*)

many places these spaces are found close to the surface (Femur, No. 1241Ba, R.C.S. Museum, Bowlby's case) (*Figs.* 131, 131A). *In a third series* there is a uniform thickening and a dense sclerosis of the shaft enclosing a contracted elongated central cavity (Femur, No. 1240, R.C.S. Museum, Paget's case) (*Figs.* 132, 132A). *The central medullary cavity* is hardly ever so much altered as to be unrecognizable. In the femur of Paget's case (late stage) it is long, well-defined, and narrower than normal. In others it may show irregularities owing to absorption of adjacent cancellous areas, or it may be broken

up into irregular large compartments by transverse septa of some thickness (No. 1241Ba, R.C.S. Museum). In the tibia already referred to (No. 1241Bn), the central cavity is filled with a network of fine trabeculæ simulating in delicacy the chordæ tendineæ of the heart, and mostly having a horizontal disposition. Quite definite changes are present in *the femoral head and neck.* The angle of the neck with the shaft is diminished in most cases—usually almost to a right angle. The cancellous tissue may be sclerosed (No. 1240).

The compact layer of the articular surface is apt to be of paper-like thinness, and may in parts be absent, a porous surface very slightly raised above the surrounding surface taking its place (Nos. 1240, 1241Ba, R.C.S. Museum). The stage reached in the neck does not necessarily correspond to that present in the shaft.

CYST FORMATION.

The formation of cysts by liquefaction of the connective-tissue new formation as in osteitis fibrosa is very doubtful in osteitis deformans. The morbid process is characterized by organizing and not retrogressive changes. Bloodgood[17] suggests that such instances as have been recorded may all have been really cases of Recklinghausen's disease (osteitis fibrosa). I have not met with a single instance in the many bones I have examined in which the cystic nature of an intra-osseous space was beyond doubt. The cavity in the cranial vault of Dr. Goodhart's patient was the nearest approach to it. The spaces frequently seen in macerated bones have probably been occupied with osteogenic tissue, or in a few instances by granulation tissue or serum associated with the absorption of a sequestrum.

From the varied picture presented by the interior of the bones in Paget's disease, it is clear that absorption of the original bone and the formation of new is the dominant feature. But the new formation is on a much larger scale than the original bone, and there is much less finish and plan in its architecture. Gross provision is made for weight-bearing by the sclerosis of the new bone, which spreads early to some depth from the surface, and eventually extends to the greater part of the whole bone; but otherwise, the incidence and distribution of the alterations are somewhat erratic—e.g., areas of absorption may be contiguous to dense sclerosis, islets of very dense bone may occur in open porous cancellous tissue, and the central cavity may escape altogether or be considerably altered.*

CLINICAL SIGNS.

The striking clinical signs which follow upon the changes in the bone texture are: (1) *Thickening;* (2) *Elongation;* and (3) *Bending.*

1. *The Thickening* usually involves the whole bone, and the increase in size may be so great that the circumference may be double that of the normal

---

* Though the chief long bones in the upper and lower extremities—not omitting the clavicle—are those usually attacked, yet the metacarpal bones and the phalanges, and probably the corresponding bones in the foot, are not immune. It is, however, rare to find them obviously involved, and, even then, only some of them are affected.

bone. When many bones are affected some may appear to be only partially involved, but the disease gradually extends to the whole bone.

2. *Elongation* can be demonstrated by measurement when the corresponding bone on the other side is free from disease; but in the case of the leg or the forearm, if only one of the bones is affected it assumes a curved form which is obviously determined by an increase of length between two fixed points. In the leg it is usually the tibia which is at fault, and it acquires a marked anterior arch whilst the fibula remains straight. In the forearm, if the ulna is free, a diseased radius is apt to become conspicuously curved in a sigmoid fashion, placing the wrist and hand in the position of complete pronation, and deflecting them to the ulnar side.[18]

3. *Bending* is first seen, and is nearly always most noticeable, in the lower extremities. The curve in the tibia is an anterior one involving the whole bone, and the femur is usually arched forwards and outwards. The patient consequently acquires a bow-legged appearance, and owing to the bending of the necks of the femora there is some degree of coxa vara which adds to his clumsiness.

Should the bones of the upper extremity bend, the convexity in the humerus is usually anterior, but in the forearm there is more variety. The two bones may be bent backwards or forwards, and there is often some explanation suggested, such as the way in which a bedridden patient is accustomed to raise the body to the sitting position, lifting a heavy patient in nursing, wringing clothes in laundry work, and so on. The shape of the thorax is determined by the bending of the ribs in front of their angles, whilst changes in the shape of the true pelvis have been described (Wilks' case). In nearly all cases the influence of weight or force is evident, but elongation is a factor which under certain conditions has just been shown to be important.

Formation of Deformities.—It is clear that the deformities which characterize Paget's disease develop in the early stages when the bone is very vascular, and the new bone-formation, which is slowly replacing the original osseous structure, is widely porous, delicate, and insufficiently calcified. It is impossible to believe that the hard, dense, sclerosed bones, so many of which are preserved in museums, could yield under any strain they might be subjected to in ordinary circumstances, and clinical evidence supports this; there was little change in Paget's case in the last four years of life.

HISTOLOGY.

The histology of osteitis deformans is very similar to that of osteitis fibrosa. The main features are the same. They are: (1) The disappearance of the original bone; (2) The substitution of a vascular connective tissue (osteogenic tissue) in place of it and its intertrabecular marrow; and (3) The formation of new bone from this connective tissue, in the first instance always by metaplasia.* But there are several notable differences which give a

* The term 'metaplasia' is used here to distinguish bone-formation direct from the connective tissue from that which is associated with rows of osteoblasts.

peculiar and distinctive character to the microscopic appearances of osteitis deformans. These are so marked that it is possible to distinguish one disease from the other by the microscope alone.

1. The first to attract attention is the *regular and even distribution* of the new trabeculæ throughout the diseased area. The whole of a section is occupied by the new osseous formations in various stages of growth, separated by comparatively narrow tracts of osteogenic tissue (*Figs.* 133, 134). In osteitis fibrosa, though trabeculæ may be comparatively crowded in parts, there will almost certainly be large areas of connective or fibrous tissue in which the traces of ossification are absent or slight. This difference is least marked in the skull bones (flat bones and upper jaws), in which the histological characters and the great hyperostosis approach more nearly to the conditions seen in osteitis deformans.

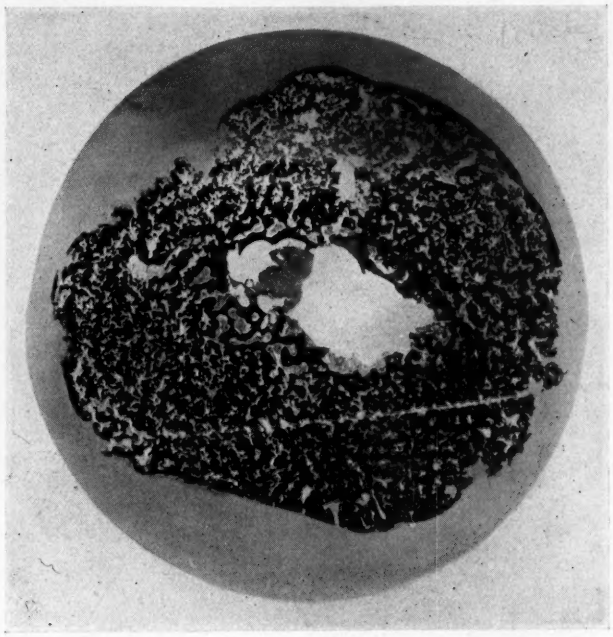


FIG. 133.—Transverse section through a clavicle (× 3) showing the regular and even distribution of the bone trabeculæ. From the same case as *Fig.* 134. The dark circumference to the section does not represent a compact cortical layer. (*College Stores, R.C.S. Museum.*)

2. Equally conspicuous is the frequency with which the *trabeculæ are seen to be decorated with internal curvilinear markings* (*Fig.* 135). Sometimes these clearly suggest a trabecula enclosed wholly or in part in a larger one, in other places they may show an outline waved and rounded like the edge of a cumulus cloud. This internal tracery is not peculiar to osteitis deformans. It may be seen, not infrequently, in osteitis fibrosa, but in that affection it is neither so pronounced nor so universal. It points to bone-formation of a later date filling up spaces outlined by earlier trabeculæ of the new formation, or fitting

FIG. 134.—Transverse section of a vertebra—from the same case as *Fig.* 133—to show the even distribution of the new bone formation. (*Photographed by Dr. G. H. Rodman from a section of Dr. Greenfields.*) (× 1·3.)

into hollows caused by giant-cell resorption. By this mode of accretion fragments of the original bone may be interlocked with, or preserved in the

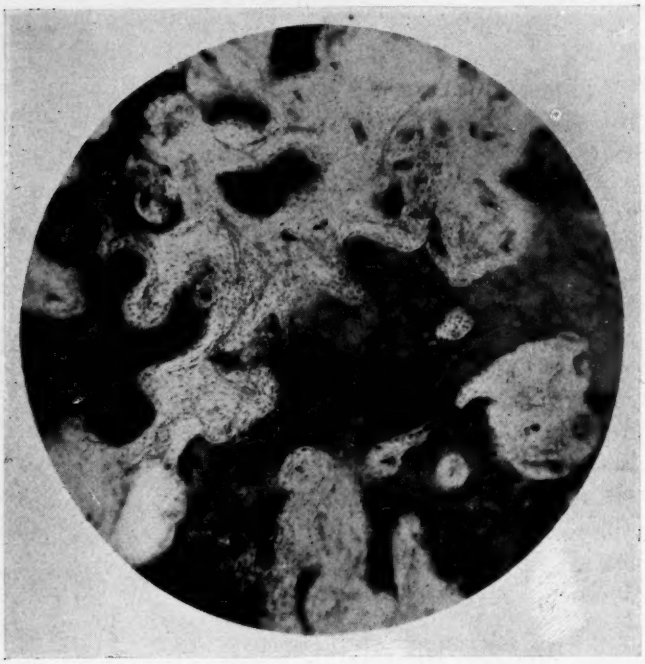


FIG. 135.—Trabeculæ from a vertebral lamina (*see case*, p. 217), showing the curvilinear markings usually found in osteitis deformans. (*Photographed by Dr. G. H. Rodman from a section of Dr. Greenfield's.*) (× 40.)

FIG. 136.—The curvilinear lines from a section taken from the skull of Dr. Hann's case. (*Photographed by Dr. G. H. Rodman.*) (× 40.)

interior of, more recent material; or, again, the point to which the disease has extended, and possibly come to a halt, may be traced by a series of

scroll-like bays on the internal surface of the original compact laminæ, filled in with more recently formed metaplastic bone. In some sections fine white lines mark part of the festooned outline, suggesting separation at the point of contact. These are probably artefacts produced in the preparation of the specimen.

Sometimes the fibrous groundwork of the trabeculæ and the confused arrangements of its whorls are as conspicuous as in some cases of fibrous osteitis. The latter, and also the internal curvilinear markings, probably originate in the following way. A trabecula, forming in the first instance by metaplasia from the connective tissue, may assume such a shape that two parts of it may come into contact, fuse, and enclose a large lacunar space filled with osteogenic tissue. Similar lacunæ may arise from the approximation and fusion of three or four trabeculæ or ossific islets. Where so little space intervenes between the trabeculæ as in osteitis deformans, it is difficult for one to increase much, especially if its growth is irregular, without coming in contact with some part of another. The formation of lacunar spaces of various shapes and sizes is therefore a necessary result of the plan of ossification. They are often spoken of as forming irregular Haversian systems—a description which is simple but confusing, for these spaces may become subdivided by the formation of smaller trabeculæ in their interior, and the further progress of many is towards complete obliteration by osseous metaplasia of their contents (*Figs.* **135, 136, 137**).

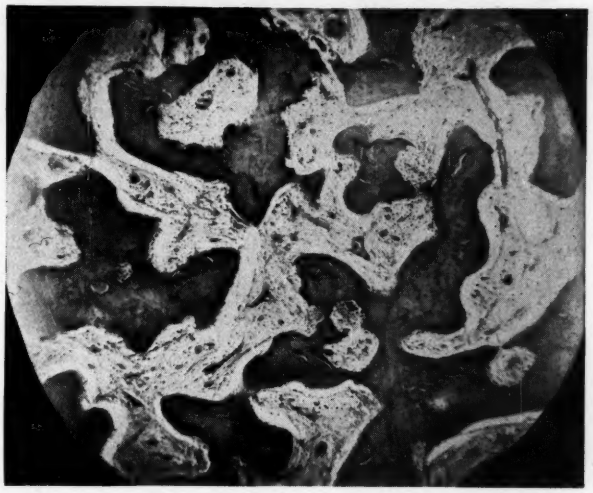


FIG. 137.—Section from the tibia shown in *Fig.* 139. The curvilinear lines are present, and the irregular plan of ossification from which they originate is well indicated. (*Photographed by Dr. O. C. Gruner.*)

Absorption by osteoclasts is in some cases extraordinarily active—much more so than in osteitis fibrosa—though in that disease it is well marked. In osteitis deformans it may sometimes be seen in progress all over the section, and it is important to realize that the newly-formed bone is being steadily attacked.

Before obliteration of the lacunar spaces takes place their circumferences may be deeply eroded in places by osteoclasts, and so the bone that fills them up may acquire a festooned or bulging outline.

3. In osteitis fibrosa the complete disappearance of fat-cells is one of the distinctive features. In osteitis deformans fat-cells are not infrequently in evidence. In the former disease the appearance of a single fat-cell attracts attention; in the latter, they may occasionally be seen, scattered or in

groups, here and there among the trabeculæ. The conversion of fat-marrow is clearly less complete in osteitis deformans than in osteitis fibrosa, probably in consequence of the greater resistance opposed by the tissues to the toxic influence. This would explain why the central cavity usually persists and is much less liable to be completely obliterated over considerable areas than in osteitis fibrosa. No doubt most of the fat-cells seen in sections are

FIG. 138.—Photograph of Mr. Littlewood's 'single bone' case, with an ulcer which led to central necrosis.

FIG. 139.—Section through the tibia of the case shown in *Fig.* 138. Showing central necrosis with incomplete separation and an aperture opening on to the base of the ulcer. (*Leeds Medical School Museum, old No.* A322, *new No.* A817.)

unchanged portions of original fat-marrow, but occasionally a suspicion that some may have resulted from reversion of osteogenic tissue to fat appears to have some foundation.

4. Lastly, there is in osteitis deformans plenty of evidence of small-cell infiltration. But the cells are lymphocytes.

3. COMPLICATIONS.

Fractures.—Spontaneous fractures, apart from growth, have been recorded in several cases. Hector Mackenzie[19] described the case of a man, age 48, an in-patient at St. Thomas's Hospital, in whom the disease had existed eight years. He was thought to have fractured a rib when turning in bed. Shortly after his right leg seemed to 'give' half way between the knee and ankle, a lump rising on the front of the tibia at the place. Another instance was recorded by Stephen MacKenzie.[20] A woman whose tibia had been bending

for a year broke both bones of the leg by slightly knocking against a stool. She did not fall.

It is astonishing that similar fractures are not more frequently reported. On several occasions I have seen in skiagrams a line of fracture extending transversely some distance into a bone from the most prominent part of the bend—evidently a cleft resulting from strain upon the convex side of the softened bone. Such clefts, when there is no local tenderness, are probably filled in with fibrous tissue, though still shown by the X rays. One at least of the cases just quoted suggests a partial fracture, and partial fractures originating in this way would easily be made complete by a slight injury. Quite recently I saw an advanced case of osteitis deformans in a man of 60 who had had five fractures in various long bones from very trivial injuries during the course of the disease. The first (of a femur) had occurred when screwing up a powerful vice some twenty years before, and was apparently due to muscular action. The others occurred in the later years.

Ordinary fractures of bones affected by the disease unite as readily as those in normal bones, though good apposition is more difficult to obtain; and those who have had experience say that they do well after operative measures.

Necrosis.—In Sir Anthony Bowlby's case (p. 209, and *Figs.* 131, 131A) a small hard sequestrum lay in a cavity about the size of a nut. Similar cavities existed in other parts of the head, neck, and shaft, but were empty Small masses of very dense bone sharply differentiated from the surrounding osseous tissue are of common occurrence in the skulls of these cases, and occasionally the appearances suggest the formation of a line of demarcation. The supervention of necrosis is best explained by the extreme condensation of the bone interfering with its circulation. Such an aseptic sequestrum may be gradually absorbed in the course of years, the cavities left being filled with granulation tissue, or possibly serous fluid.

Another variety was met with in the tibia in Littlewood's case (p. 209, and *Figs.* 138 and 139). A sinus led from an ulcer into the central portion of the lower end, and when the bone was bisected a partially separated green necrotic mass of rarefied cancellous bone—evidently of the new formation—was found in its interior. The ulcer had formed long after the disease had declared itself, and the septic osteomyelitis was evidently the result of infection from it. The track of infection was probably prepared by the substitution of open porous bone for the compact tissue, so that the connective tissue medulla would come into immediate continuity with the septic surface. This case emphasizes the importance of careful treatment of ulcers overlying bones affected by this disease. (Leeds Medical School Museum, No. A322, new No. A817.)

Ulceration or Discoloration, or both, of the tissues overlying the tibia, is not infrequent. It may be explained by impaired nutrition of the skin and superficial structures, which results from the changes in the bone and the retarding influence of muscular atrophy and diminished activity upon the venous return.

Atheromatous Arteries are almost a constant feature in these cases, and seen even when the disease occurs in early middle age. The arterial disease

does not interfere with an adequate blood-supply to the bones, for in the early stage this is excessive; nor is it likely that the atheroma is in any degree responsible for the bone changes, though this idea has been mooted. But it is quite possible that the deforming osteitis, the atheromatous changes in the vessels, and the gout, which these patients are said often to suffer from, may have a common exciting origin in toxins—possibly of intestinal or metabolic origin.

Osteo-arthritic Changes in the joints have occasionally been described (Lambert,[21] four cases). They do not appear to have been advanced, and when present were probably an accidental association. They are probably not more common than in other elderly folks, though the changed mechanics of the joints may sometimes favour their onset. Other accidental (?) troubles that have been recorded are lunacy (Beadles, Lambert), Huntington's chorea (Mackey), syringomyelia, and deafness (Jenkins).

Malignant Disease.—The frequency with which malignant disease supervened in his cases made a deep impression upon Paget, and the cases that were recorded soon after gave confirmation to the belief, that is even now widely held, that osteitis deformans usually, or at least very frequently, terminates by some malignant complication. And this view would gain support from the relative number of such specimens in museums. On the other hand, there is reason to believe that the frequency of this complication has been accidentally exaggerated. Packard[22] pointed out that in 66 cases there were only 8 of malignant disease, and 2 of non-malignant tumours. Gruner[23] states that up to 1902 only 14 of the recorded cases were associated with tumour formation (carcinoma 4, sarcoma 5, either carcinoma or sarcoma 4), whilst since 1902 (i.e. in more than one half of the reported cases) Higbee and Ellis[24] found mention of only 2 benign tumours. No doubt these figures do not represent the exact state of affairs, for many recorded cases were alive when described, and some malignant cases represented in museums have not been recorded. They afford, however, sufficient evidence to show that the first impression on this point must be readjusted.

When malignant disease does complicate osteitis deformans it is apt to appear more often than not in a bone which has not been obviously altered, or at any rate much altered, by the disease. Moreover, in a fair proportion of cases its connection with the bone disease is very doubtful (Wilks: epithelioma of internal surface of the dura. Goodhart: lymphomatous masses in liver, spleen, glands of mediastinum and abdomen; no primary source found. Robinson: sarcoma of cerebellum).

When it occurs in the bones it is usually in the form of an endosteal tumour; but if it arises in the cortical portion of the bone it projects prominently on one side and gives the impression of a periosteal origin (Univ. Coll. Hosp. Museum, No. 651A, Bone 64G).

4. PATHOGENESIS.

It is interesting to note that osteitis deformans was very soon thought to be of toxic origin. Sir Jonathan Hutchinson[25] believed that it was "simply an infective osteitis, and that granting certain constitutional peculiarities it

was probable that the disease usually began as a consequence of contusion in one bone and spread by infection to others". Evidently he used the term 'infection' in the same sense as we should employ the word 'toxins', for further on he adds, "The theory, put concisely, is this, that the products of inflammatory action in any tissue are, when circulating in the blood, infective to that tissue throughout the body".

A different explanation of the toxæmia was suggested by Oetlinger and Lafont. They thought that the disease, which they met with in two brothers, whose father also had probably suffered, might be due to intoxication by mineral acids owing to the chlorine-laden atmosphere of the workroom in which they followed their occupation of laundrymen. The ingestion of hydrochloric acid would reduce the alkalinity of the blood, and set free indirectly a great quantity of lactic acid which would affect the evolution and structure of the bone. Their argument was supported by a table of the occupations of quite a number of cases in which the conditions were such that a similar explanation might be advanced.[26] At the present time this lactic acid theory cannot be seriously entertained.

Another theory was advanced by Gilles de la Tourette and Marinesco.[27] They found changes (atrophic, not true sclerosis) in the posterior median columns of the dorsal cord, and suggested that the bone troubles were trophic. Commenting on this idea, Packard writes, "The absence of all clinical evidence of trouble in the nervous system, and the results of many examinations which have shown the cord and bone nerves (von Recklinghausen) to be perfectly normal, render it unlikely that the lesions referred to have anything to do with the origin of the condition".

The possibility of the disease being due to micro-organic infection has, of course, been thought of. There is, however, a dearth of bacteriological investigations, and those that have been recorded are contradictory. J. C. Da Costa[28] writes, "Several Italian scientists claim to have found a diplococcus in the bone, and assert that they have found a similar diplococcus in the bone of osteomalacia. They prepared a vaccine and claim to have proved it serviceable. In two of my cases I removed a bit of bone from the tibia. Dr. Ellis made a careful study and found each piece of bone sterile. Beyond the statement of the Italian scientists there seems to be no evidence that bacteria can be causal". Levin[29] gives this additional information: "Da Costa, Funk, and others have tried to make a vaccine, but culture and animal inoculation experiments were negative". Morpurgo, Archangeli, and Fiocca were no doubt the Italian investigators to whom Da Costa referred.

The Toxic Theory Considered.—Proof of the toxic theory is at present impossible, but the known facts are more in harmony with it than with any other: (1) There is an absence of any reliable evidence that the condition is due to micro-organic infection. (2) Adami,[30] in discussing the nature of chronic inflammation, points out that the process is long-continued and is accompanied by few or none of the cardinal symptoms of inflammation; that proliferative changes are more prominent than the vascular disturbances, and that the evidence of leucocytic migration is slight. Such changes when not of bacterial origin may be the result of repeated slight mechanical injuries or more often the effects of perverted metabolism and continued slight

intoxications affecting particularly certain tissues. The change in the medullary tissue in osteitis deformans conforms to this description, and there can be little doubt that it is brought about by toxic irritation. At the present time opinion certainly trends in this direction and attributes the origin of the toxins to tissue metabolism, or to the absorption of poisons of similar origin from the intestinal tract. Tubby[31] mentions a very suggestive case. It was that of a medical man who attributed improvement to the adoption of a diet rich in proteins and very sparing in carbohydrates, and the whole malady entirely to error in diet, viz., to lack of protein mainly, but partly to excess of starch. Eating potatoes never failed to produce a return of his pain.

In my Hunterian lecture on osteitis fibrosa I dwelt at some length upon a second important factor in its pathogenesis, viz., *the power to resist toxic influence inherent in the bones themselves.* That disease was assumed to depend upon an individual idiosyncrasy which permitted the bones to suffer damage from certain noxious blood-borne substances that produced no ill effects in ordinary people. The same assumption holds in the case of osteitis deformans. The toxins responsible for it can excite it only in the susceptible. On this hypothesis its sporadic incidence can be accounted for, and inherited tissue proclivity, which is probably the cause of the familial type, explained.*

5. THE CORRELATION OF OSTEITIS DEFORMANS, OSTEITIS FIBROSA, AND OSTEOMALACIA.

When describing the histology of osteitis deformans I could not help concentrating attention upon the close resemblance that the microscopic appearances present to those of osteitis fibrosa. The essential characteristics were the same; any detectable differences were a matter of degree.

In considering the relations which exist between osteitis deformans, osteitis fibrosa, and osteomalacia, the pathological process, with which all three are intimately concerned, should be constantly borne in mind. That process, as I conceive it, begins by the entrance of certain toxins into the circulation. These toxins of metabolic or intestinal origin (?) are carried by the vessels to the bones and diffused by the lymph. The effect produced on the different constituents of the bone varies. The osseous framework, being a more vulnerable tissue than the marrow, has its vitality depressed beyond its power of recovery, but the connective-tissue basis of the marrow is excited to remarkable activity. The reaction which the toxic injury originates is shown by the striking alteration in the marrow. It is changed into an actively growing vascular connective tissue, whilst the fat vanishes from the cells, or the fat-cells themselves disappear. This new tissue plays a twofold part: (1) through its agency the damaged bone breaks up and disappears; (2) it becomes busily engaged in the manufacture of fresh bone by the metaplasia of its own fibrils and cells.

It should be noted that resorption, even of the new bone, is always going on, and sometimes is so widespread and active as to suggest a continuous

---

* There are three instances of a father and son becoming affected, and one of two brothers, two of a mother and daughter, and another of brother and sister. (Oetlinger and Lafont.[26])

action of the toxins. At one time the reactionary soft tissue in the bone is probably largely in excess of the contemporary bony framework; but ossification, especially in osteitis deformans, outruns resorption. Howship's lacunæ, and lacunar spaces formed by the coalescence of trabeculæ, are speedily filled with new bone, and rows of osteoblasts are now seen behaving normally. In this way the bone may be reconstituted.

I would next point out certain peculiar features of this reaction in the case of osteitis deformans which seem to indicate that the bones in that disease are less seriously affected by the toxins than in osteitis fibrosa. These peculiarities are as follows: (1) the original bone is often not so completely removed as in osteitis fibrosa; (2) the reaction is apt to extend not so deeply into the fat marrow—the persistence of the central cavity in the long bones may be taken as an evidence of this; (3) it may be inferred from the regularity of the distribution of the new trabeculæ that the ossifying function is more vigorous, i.e., has been less depressed; (4) the interference with the strength of the bones is slower and less grave.

An explanation of the better defence against toxic influence put up by the bones in osteitis deformans may be found in their greater power of resistance. Vital resistance is here implied, but the greater strength and density of the mature adult bones as compared with those of childhood and adolescence must not be overlooked. Two clinical facts also throw light upon this matter. *The first* is concerned with the age at which the two diseases begin. Osteitis fibrosa is a disease of young people. It starts in the first or second decade of life. Osteitis deformans, on the other hand, is an affection of middle or old age. It rarely begins before the end of the 4th or the beginning of the 5th decade, and it may develop at any time between that and old age. *The second* is, that the subjects of osteitis deformans usually show marked evidence of arterial degeneration. The argument, therefore, leads to the inference that a *susceptible* individual with a sufficient reserve of resisting power may stave off osteitis fibrosa in youth, but succumb to osteitis deformans in old age when that resistance has been undermined by failing vitality and disease.

This view of the close connection between osteitis deformans and osteitis fibrosa will help to clear up some of the confusion that exists with regard to them. In well-marked cases the diagnosis need never be in doubt; but there are cases—intermediary cases, perhaps—in which it is. I have already referred to a clavicle (No. A119b, Leeds Medical School Museum) supposed to be an example of osteitis deformans, and whose appearance does not belie that diagnosis. But microscopically it is osteitis fibrosa. The patient was a young woman 19 years of age, and *age will be found to be a very useful indication.* Radiologists, also, meet with and are puzzled by cases of undoubted osteitis deformans in which, in some parts of the skeleton, appearances are found which they are accustomed to associate with osteitis fibrosa. If the above explanation is sound, there is no inherent improbability of the occasional association in a single individual of lesions typical of both conditions.

But if osteitis fibrosa and osteitis deformans are to be looked upon as simply different expressions of the same disease determined by the dissimilar resisting powers of their victims, what then is the position of osteomalacia,

another toxic bone disease, which presents very different clinical as well as pathological phenomena ?

Is there any connection between that affection and the other two ? I believe there is, and will now give the reasons for my belief that the three conditions have a very similar—probably an identical—origin, and that, just as osteitis fibrosa or osteitis deformans is determined by some inborn property of the individual, so osteomalacia is similarly to be explained.

The clinical signs which are common to all three conditions—viz., softening, bending, and fracture of the bones—may be dismissed as of little importance in establishing this relationship. But if the histological features of the three diseases are contrasted, a very significant conception is suggested. A description has just been given of the effect on the bone tissue of the toxic insult and of the reaction which it induces in the more recuperative marrow. In both osteitis fibrosa and osteitis deformans this reaction is very marked; the marrow is completely altered over large areas, and ossification in it is active. But in osteomalacia this reactionary change in the marrow is only developed to a slight extent, except under the stimulus of fracture or in the case of recovery taking place. In histological sections the dissolving and disintegrating trabeculæ may be seen to be surrounded only by narrow zones of newly-formed connective tissue, and outside these zones tracts of ordinary fat marrow persist. There is no sign of ossification in this connective-tissue environment: bone disintegration alone is going on. (*Fig.* 140.)

FIG. 140.—Microscopical appearances in a section from an osteomalacic bone, showing trabeculæ with decalcified borders, surrounded by proliferated connective tissue, but with normal medulla and fat persisting between the connective-tissue zones. There is no sign of active ossification. (*From a case of Mr. F. H. Mayo's, of Leeds. Photographed by Dr. O. C. Gruner.*)

These two facts seem to point to a degree of reaction so slight, that for the purpose of this argument reaction may be regarded as practically absent. In osteomalacia, then, it would seem that the tissues have not the power to react to toxic injury. Consequently, when the osseous framework disappears, the tissue replacing it, being possessed of too little vitality to maintain its own existence, or to advance to better things, peters out in fatty degeneration. Why should there be this failure to react ? Surely the answer is to be found in the depressed and enfeebled condition of those in whom osteomalacia develops. Many who suffer from it have been subjected to debilitating influences such as poverty, privation, anxiety, rapid and repeated pregnancies, and residence in unhealthy dwellings and damp localities. This depressed vitality is one of the marked clinical features of osteomalacia.

It is important also to recognize that the course of osteomalacia is not infrequently punctuated by periods of apparent or partial recovery. If systematic examination of the bones of such a case were made, evidence

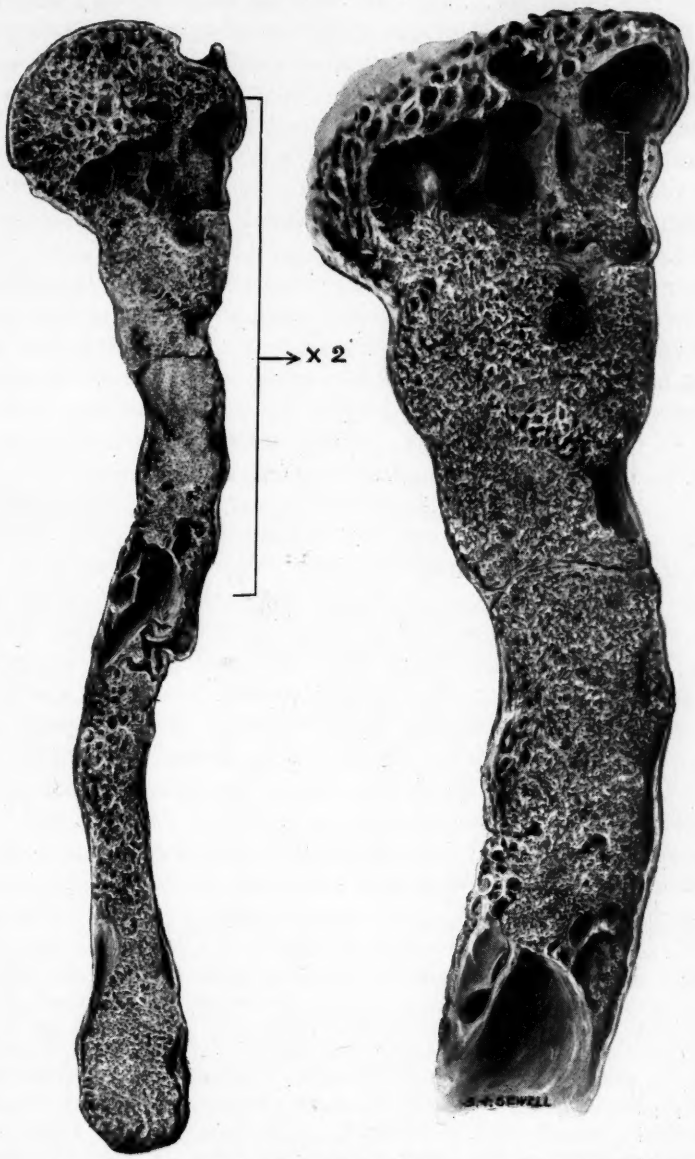


FIG. 141.—Drawing of the dried half of the humerus described in the text; Goodwin's case. The picture on the right is a × 2 magnification of that part of the left figure included in the brackets. It shows the fine bony network which is made visible by the drying. In this case the part below the articular cartilage showed the microscopic appearances of osteomalacia, and a section cut from the surgical neck those of osteitis fibrosa. *No.* 735, *R.C.S. Museum.*)

of reaction would be found, and possibly osteomalacic changes and osteitis fibrosa could be demonstrated in the same skeleton or in the same bone. This combination has been found in one of Hunter's original preparations.

In the Royal College of Surgeons' Museum are the two halves of a humerus which has been divided vertically, Nos. 734 and 735. One half has been mounted as a wet specimen, the other as a dried one (not macerated).

The wet specimen, No. 734, "the subject of mollities ossium", shows a fracture at its lower end. The bone is of natural shape, but except for a very thin and rarefied cortex, and for a small amount of cancellous tissue adjacent to the articular cartilages, it is composed of a pale, soft structure which feels fibrous and gritty.

The dry specimen, No. 735 (*Fig.* 141), is "shrivelled into a tough flexible mass like a piece of dried muscle". Its interior is filled from side to side and from end to end—except where it is interrupted by a cystic space—with a very fine reticulated osseous tissue.

Professor Shattock picked a spicule from the cancellous tissue just below the upper articular surface of No. 734, and carefully prepared it without artificial decalcification. It showed the characteristic histological appearances of osteomalacia, viz., a typical double contour to the trabeculæ due to a calcified central portion surrounded by a decalcified border; also a granular appearance of the central calcified portion, and the lacunæ surrounded by a pale area with innumerable lines radiating laterally.

He next prepared a longitudinal section cut from the surgical neck (734), including the periosteum and a considerable depth of the gritty fibrous interior, and stained it with eosin and hæmatoxylin. The chief portion of this specimen was typical of osteitis fibrosa. A regular network of newly-formed trabeculæ spread through a continuous field of connective tissue. The trabeculæ were only partially calcified, the lime salts being deposited irregularly in an acalcified matrix, and they were being formed from the connective tissue without the mediation of layers of osteoblasts. The subperiosteal cortical layers were long and atrophic, without any decalcified bordering, but the spaces between them were filled with fat—a condition not inconsistent with an interrupted osteomalacic process.

The case was published by Goodwin,[32] and Hunter gave an account of the dissection of the arm which had been sent to him.[33]

The patient was a woman, age 34. After suffering from severe rheumatic pains in the limbs, she broke her leg tripping against a brick. She soon after became pregnant, and broke her left femur getting out of bed. She was safely delivered, but suffered several more fractures, and again becoming pregnant she gave birth to a living child. Subsequently her health improved, but during another pregnancy (the tenth) the fractured bones, which had united, broke again, the dissolution of the callus being preceded by excruciating pain. Several new fractures then occurred, and on her death after three years' illness the bones were found to be so soft that they could easily be cut with a penknife. The cranium and vertebræ were much affected, and the bones of the lower extremities were the least diseased.

From an observation of Ziegler's in connection with the description of osteomalacia, that "new osteoid tissue is not infrequently found in bones which have not perceptibly bent or yielded",[34] it is evident that similar facts have been recognized before; and from such facts and from the structure of callus in these cases the conclusion naturally follows, that when recovery does take place in osteomalacia the bone changes characteristic of that condition give place to those of osteitis fibrosa.

The argument may be summarized as follows :—

1. Certain diseases of the bones owe their origin to the action of toxins—probably those of metabolic or intestinal origin.

2. Predisposing to their development an idiosyncratic susceptibility on the part of those who suffer from them may be assumed.

3. The ability of the bones to resist toxic influence is a factor of great importance.

4. The relative intensity of that resistance can be roughly gauged by the extent and character of the reaction excited in the soft tissues of the affected bones.

5. If the vitality is good, the resistance opposed to the toxins may ward off harmful effects till the constitutional strength is reduced by age and disease. The reaction under these circumstances is strong, and the resulting affection takes the form of *osteitis deformans*.

6. On the other hand, if vitality is feeble the disease appears earlier—in childhood, adolescence, or early manhood. The reaction is fair, but not so vigorous as in osteitis deformans. The form the disease then assumes is that of *osteitis fibrosa*.

7. Lastly, when owing to the severe depression of the patient's vitality, usually by untoward circumstances, the power to react is absent *osteomalacia develops*.

6. CAUSES THAT MAY DETERMINE THE ONSET OF THE DISEASE.

The onset of osteitis deformans appears with some frequency to be determined by an accidental circumstance or condition which no doubt causes some local or general depression of vitality. Injury is the most important of these predisposing causes. It is said to be particularly frequent in the single bone cases (*see* p. 209), but it is often mentioned in the records of cases of generalized disease. Inflammation of the skin over both legs was suspected in one case. It lasted four or five months, and left large pigmented areas when it subsided. Five years later the first signs of the disease appeared in the legs,[35]

The following history was given by a man, age 58, under the care of my colleague, Mr. J. A. Coupland, at the Leeds General Infirmary, with an enlarged bent tibia—the only bone affected. Twenty years ago he sprained his knee. When 40 years of age he sustained a fracture (?) just above the ankle, which he treated himself. Eight years ago he suffered with blood poisoning from a wound caused by a rusty wire. The leg was enormously swollen, and marks of more than a dozen incisions were present. The leg was noticed to be bending from that time, and more so in the last five years. (From notes by Mr. A. W. Birtwistle.)

Overfatigue, fatigue from long nursing, injury with attendant fright, frequently getting wet through, have all been thought to exert a predisposing influence in particular cases ; and, indeed, any debilitating illness, whether of micro-organic origin or not, might act in this way.

A history of syphilis has been present in a few cases (Paget[36]) ; but it

is rare for this to be obtained or for any sign of that disease to be found. Da Costa[37] states with reference to the Wassermann tests that " four-fifths of the cases have a negative reaction ". " A consistent positive reaction has never been found in an uncomplicated case ".

Internal Glandular Secretions.—As these secretions are undoubtedly associated with certain bone conditions, it is natural that cases of osteitis deformans should be carefully scrutinized for any evidence of their influence. The facts that have been gleaned have been considered by Hurwitz, and by Higbee and Ellis, and the opinion of the former,[38] which appears to be well founded, is " that the assumption that there is a causal connection between the internal secretions and osteitis deformans is mere speculation ".

The Nature of the Morbid Process.—From the beginning it has been regarded as inflammatory. Paget and Butlin discussed this point at length in the original paper, and were decidedly of that opinion. Adami and MaCrae[39] find no evidence of the inflammatory stage and regard the process as metaplastic. This has reference to the alteration of the medulla from fatty or abundantly cellular to fibroid, but hardly coincides with Adami's observation on chronic inflammation which I have summarized in discussing the toxic theory. This question was dealt with in my lecture on osteitis fibrosa, and the same reasons that were held to indicate that that affection was inflammatory apply in the case of osteitis deformans.

I wish to acknowledge the debt of gratitude that I owe to the late Professor Shattock in connection with this lecture. Always kind, sympathetic, and approachable, it might almost be said that it was prepared under his supervision. My thanks are also due to the curators of the different museums from which I have drawn my material, and to others, for their kind help and courtesy, and to Dr. G. H. Rodman for the pains he has taken to bring out in the microphotographs the points which I wanted to make, and to Messrs. George, Steward, and Wilson, of the Royal College of Surgeons staff, for their valuable help, which is evidenced by the illustrations. Nor must I forget the kindness of Dr. O. C. Gruner, though it is many years since he took the plates which I have now made use of.

REFERENCES.

[1] PAGET, *Brit. Med. Jour.*, 1882, Dec. 16.
[2] PAGET, *Trans. Med.-Chir. Soc.*, 1877, lx, 37.
[3] WILKS, *Trans. Pathol. Soc. London*, 1869, xx, 273.
[4] CLUTTON, *Ibid.*, 1888, xxxix, 261.
[5] GRIFFITHS, *Ibid.*, 1891, xlii, 249.
[6] WHERRY, *Brit. Med. Jour.*, 1896, Sept. 19.
[7] GOODHART, R.C.S. Museum, 705.1, Gen. Path. Section.
[8] RULLIER, *Bull. de la Fac. de Méd. de Paris*, 1809, ii, 94 ; *Catalogue Musée Dupuytren*, 1877, ii, No. 453.
[9] LUNN, *Trans. Clin. Soc.*, 1885, xviii, 272.
[10] BOWLBY, *Trans. Pathol. Soc. London*, 1883, xxxiv, 192.
[11] *Med.-Chir. Trans.*, lxv.
[12] HURWITZ, *Johns Hop. Hosp. Bull.*, xxiv, 263.
[13] BEADLES, *Edin. Med. Jour.*, 1898, iii, N.S., 388.
[14] WYLLIE, *Brain*, 1923, xlvi, 336.
[15] *Ibid.*

[16] Greenfield, J. G., *Jour. Neurol. and Psychopathol.*, 1921, ii, 116.
[17] Bloodgood, *Ann. of Surg.*, lii, 163.
[18] St. Thomas's Hosp. Museum, No. 415B ; Clutton, H. H., *Trans. Pathol. Soc. London*, xxxix, 261 ; Symonds, C. J., *Guy's Hosp. Rep.*, 1881, Ser. 3, xxv, 99.
[19] Mackenzie, Hector, *Trans. Clin. Soc.*, xxix, 245.
[20] MacKenzie, Stephen, *Ibid.*, xviii, 331.
[21] Lambert, *Bull. of Committee for Study of Special Diseases*, ii, chap. xxii, 75.
[22] Packard, Steele, and Kirkbride, *Amer. Jour. Med. Sci.*, 1901, cxxii, 552.
[23] Gruner, Stringer, and Foster, *Arch. of Internal Med.*, 1912, ix, 641.
[24] Higbee and Ellis, *Jour. of Med. Research*, 1911, xix, 55.
[25] Hutchinson, Sir Jonathan, Bradshaw Lecture, *Illus. Med. News*, ii, Feb. 23, 99.
[26] Oetlinger and Lafont, *Nouvelle Iconographie de la Salpêtrière*, 1905, xviii, 292.
[27] Gilles de la Tourette and Marinesco, *Bull. Soc. méd. Hôp.* xi, 422, and xii, 789 ; Morton Prince, *Amer. Jour. Med. Sci.*, 1902, cxxiv, 810.
[28] Da Costa, *Surg. Clin. N. America*, 1921, Feb., No. 1, 55.
[29] Levin, *Jour. Bone and Joint Surg.*, 1922, iv, 51.
[30] Adami, *Principles of Pathology*, i, 401.
[31] Tubby, *Deformities : Including Diseases of the Bones and Joints*, 1912, ii, 569.
[32] Goodwin, *London Med. Jour.*, vi and viii.
[33] Hunter, *Ibid.*, viii, 70.
[34] Ziegler, *Text-book of Special Pathological Anatomy*, trans. 3rd ed., 1896, i, 149.
[35] *Johns Hop. Hosp. Bull.*, 1898, ix, 135.
[36] Paget, *Trans. Med.-Chir. Soc.*, lxv.
[37] Da Costa, *Surg. Clin. N. America*, 1921, Feb., No. 54.
[38] Hurwitz, *Johns Hop. Hosp. Bull.*, 1913, xxiv, 273.
[39] Adami and McCrae, *Text-book of Pathology*, 789.

A CONSIDERATION OF TWO CASES OF CYSTADENOMA OF THE PANCREAS, AND THEIR PROBABLE RELATIONSHIP TO POLYCYSTIC CONDITIONS FOUND IN OTHER VISCERA.*

By E. ROCK CARLING and J. A. BRAXTON HICKS, London.

CLINICAL NOTES.

The first case, W. C., a male, age 53, a patient of Dr. C. H. Pring, had been treated for hæmoptysis in 1922. No tubercle bacilli found in the sputum. In September, 1924, feeling 'out of sorts' but having no definite symptoms, he consulted Dr. Pring, who found glycosuria. On a restricted diet the sugar quickly disappeared. Seen in November by one of us (E. R. C.) with Mr. Arthur Evans, he complained of nausea and abdominal pain. He had not lost flesh. In the epigastrium, mainly to the right of the middle line, was a hard tumour of rounded outline, dull on percussion, apparently separable from the liver. No jaundice, and stools of normal appearance. Mr. Evans thought the lump pancreatic, but there was also some question whether it was not a malignant growth of the stomach or transverse colon.

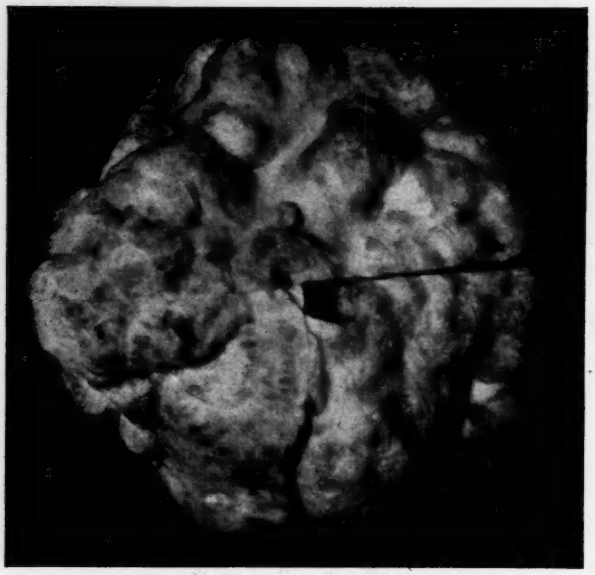


Fig. 142.—Cystadenoma of the pancreas removed in *Case* 1. Situated behind the lesser sac, between stomach and liver, the actual attachment to the pancreas was by a pedicle of not more than ¼ in. wide; the pancreatic tissue exposed was slightly spongy in texture.

Exploratory laparotomy (E. R. C.) revealed a cystic tumour between stomach and liver, about 4 in. by 4 in. by 2½ in. It was found that, when freed from all other connections, the tumour arose by a narrow pedicle from the upper border of the head of the pancreas, near the mid-plane of the body. (*Figs.* 142, 143.) After removal a drain was left in, and from a purely surgical point of view there was no trouble. Pneumonia set in, and very severe glycosuria. The hyper-

* From the Laboratories of the Westminster Hospital.

glycæmia fluctuated violently and was very imperfectly controlled by insulin, despite repeated estimations of the sugar content of the blood. Death supervened on the tenth day.

The second case was that of F. B., male, age 76, under the care of Mr. William Turner, to whom we are indebted for permission to publish these notes. Admitted April 24, 1922. For eighteen months he had been aware of a lump in the abdomen, and had been losing flesh. Three months before admission he had had an attack of severe abdominal pain, during which, for a fortnight, he was very ill. Since that date he had had increasing constipation. Temperature, pulse, and respiration were normal.

FIG. 143.—Sectional view of the tumour illustrated in *Fig.* 142.

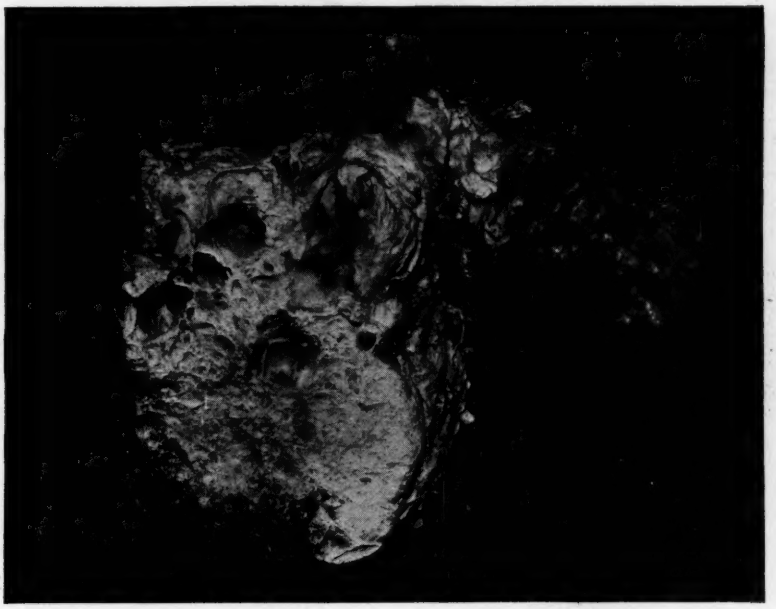


FIG. 144.—Post-mortem specimen. Pancreas containing cystadenoma; from the case of F. B., under the care of Mr. William Turner. (*P.M.* 30–213.)

A large hard tumour occupied the right hypochondrium, extending into

the right lumbar and epigastric zones. Its lower margin could be defined, and projecting backwards from it were two rounded masses the size of oranges. The diagnosis was "probably metastases in the liver, from carcinoma of the hepatic colon", but in view of the recent acute attack of pain, etc., the possibility of an inflammatory mass from some lesion of the gall-bladder or in its neighbourhood was also considered.

Laparotomy revealed a cystic mass in and below the pancreas, the cysts containing a glairy fluid. A mass of adhesions in the upper part, binding down the colon to the liver, was regarded as the result of peritonitis from rupture of one of the cysts, at the time of the acute illness.

The patient died seventeen days after the operation, and at the necropsy the ovoid tumour illustrated in *Fig.* 144, 6 in. by 4 in., was found replacing

FIG. 145.—Section from the tumour in *Fig.* 142, showing the low cuboidal cells lining the cyst spaces. Where these cells can be seen free they have a polyhedral form, ample clear protoplasm, and a large deeply-staining single nucleus. The ground substance of the tumour is connective tissue, in places cellular, in others well-formed fibrous tissue. (*C.R.* 21–882; *Section No.* 4109A.)

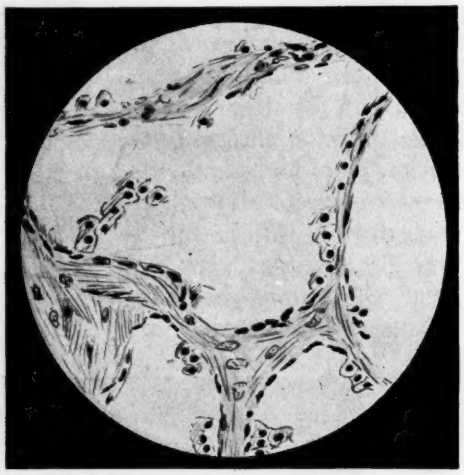


FIG. 146.—Section of tumour shown in *Fig.* 144. As contrasted with *Fig.* 145 it will be seen that the ground substance is scanty, but that the general arrangement, and the type of cell lining the cysts, are closely similar. (*P.M.* 30–213. *Section No.* 3679A.)

the head of the pancreas. The body and tail were normal, though the duct, which passed right through the mass freely into the duodenum, was dilated. The central portion of the tumour was calcareous, and the whole weighed 36 oz. It was adherent to and pressed on the colon, but there was no evidence of 'infiltration' or of secondary deposits.

Microscopical examination of these two tumours (*Figs.* 145, 146) reveals a striking similarity between them, so much so that one can at the outset assume that the pathological conditions are the same in each case. There are, it is true, individual peculiarities, but these are rather in degree of tissue changes than in actual type of tumour. Thus the basic appearances seen are those of a coarse network of fibrous or fibromuscular trabeculæ enclosing spaces lined with cells of polyhedral, low cuboidal or flattened types. There is no

suggestion of 'malignancy' in the accepted histological sense; there is not the slightest resemblance in the structure of these tumours to the normal or even malignant pancreatic cell arrangement; and what seems to us very

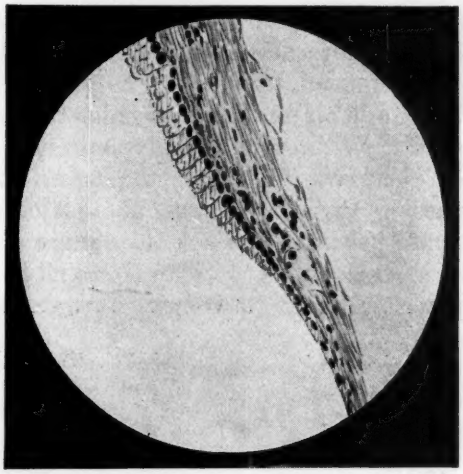


FIG. 147.—Part of the wall of a 'solitary' cyst enucleated partly from the upper aspect of the head of the pancreas, partly from the wall of the pyloric portion of the stomach. The wall is like that of the other cysts; the lining cells, columnar at one part, become low cuboidal, and eventually flattened, as the wall becomes thinner. This particular area of the section is, of course, specially chosen as illustrating the changes columnar epithelium undergoes either under pressure or in association with stretching of the connective-tissue wall. (*C.H.*; *Clin. Rep.* 20–1116; *Section No.* 3884A.)

important also, no connection with the pancreatic ducts. The last factor was partly exemplified by the ease with which a probe passed through the pancreatic duct into the duodenum, through the whole of the main mass of

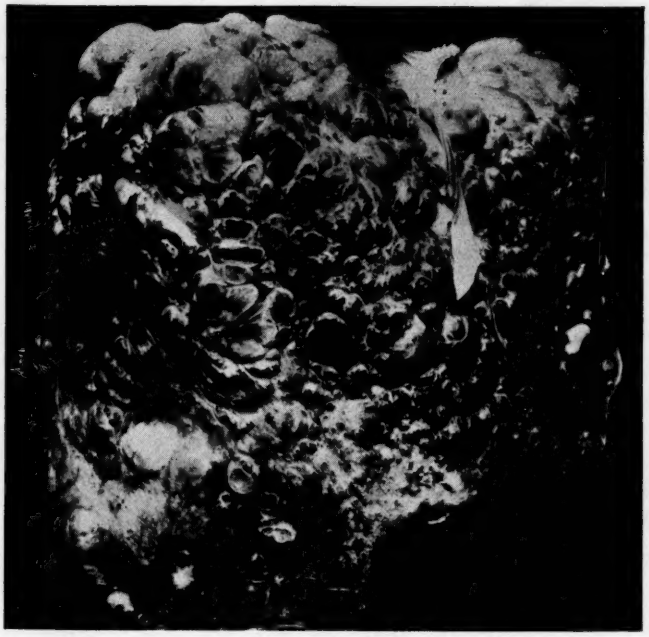


FIG. 148.—Liver of A. W., a patient of Mr. W. G. Spencer's. Weight 167 oz. Polycystic disease of the liver and kidneys. The case was admitted as an acute abdominal emergency; severe pain, great distention, complete constipation. The post-mortem report states that death was due to hepatic and renal inadequacy. The kidneys, right 36 oz., left 39 oz., were typical examples of polycystic disease. (*Sections* 1264A to 1268A; *P.M.* 27–42.)

the tumour, in the case **F.B.** In the same case there was a suggestion that these cystic spaces might have arisen as lymphatic spaces of new formation, but a consideration of the whole tumour (or of both tumours) in

our opinion negatives such a suggestion; indeed, the only difference between the pancreatic tumour in the two cases is that the cystic spaces in the first are larger and more irregular in size and shape than are those of the second, in which the texture is much more like a close-meshed sponge.

It is interesting to note that in a solitary cyst which was embedded partly in the pancreatic substance and partly in the muscular wall of the stomach, and removed by one of us (E. R. C.), similar appearances can be found. There is a wall of fibromuscular tissue; the lining cells vary from tall columnar with a well-marked deeply-staining nucleus to partly flattened cells. Further, in one part (*Fig.* 147) the transformation from the one type to the other, passing through a low cuboidal cell stage, can be seen, and this change is found where the thick fibromuscular wall becomes attenuated. Moreover, even this 'solitary cyst' contains in some parts of its wall smaller cysts of precisely the same structure as the main cyst.

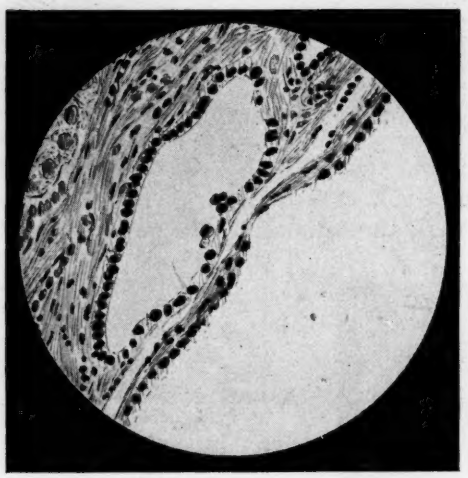


FIG. 149.—From the liver illustrated in *Fig.* 148. The similarities between this and the section in *Fig.* 150 do not need particularization. (*P.M.* 27–42; *Section No.* 1264A.)

FIG. 150.—From the kidney of the same case as *Fig.* 149. On the upper edge of the drawing the lining cells of a cyst of medium size. Many have apparently double nuclei, but they are otherwise similar to those in the other cysts. (*P.M.* 27–42; *Section No.* 1267A.)

In our investigation of these three tumours, we were led by their very similar appearances to reconsider the structure of such examples as the one illustrated showing polycystic disease of the liver and kidneys (*Fig.* 148), and a similar one, formerly under the care of the late Mr. Charles Stonham, in the Museum of the Hospital (No. 563, in Museum Catalogue), in which also both liver and kidneys were involved, the liver to a very much less degree than our illustrated case; and still further to consider their probable relationship to a case of cystadenoma of the bile-ducts published from this laboratory by Mr. Arthur Evans.[1] In the case of polycystic disease of the liver, though the connective-tissue walls (or, perhaps more correctly, the connective-tissue masses in which the cysts are embedded) are very much more cellular, and much less definitely fibrous in type, than those of the pancreatic cases, yet the

cells lining the cystic spaces are of closely similar appearance to those seen in the pancreatic tumours, and indeed do not differ materially from those seen lining the spaces in the kidneys of the same case; it would be possible to place under the field of the microscope a part of any one of these cysts, save possibly the renal, and mistake it for any other. This has become very apparent to one of us (E. R. C.) during the process of drawing the appearances for the illustrations reproduced (*Figs.* 149, 150).

In the case of the cystadenoma of the bile-ducts referred to, the cells lining the ducts are of a very tall columnar type, with nuclei elongated in the axis of the cell (*Fig.* 151). They do certainly suggest an origin from bile-ducts, but the tissue in which the cysts are embedded is not liver parenchyma, but of a fibrous nature; nor have we ever established any connection between the cysts and existing bile-ducts. Further, these cysts did not contain bile. The patient, after the first operation, did not make any great progress towards recovery; the liver became irregularly enlarged, and was of enormous size when the patient died. Unfortunately permission for a post-mortem was refused, and we are indebted to Mr. Arthur Evans for these further notes on his case. It is our belief that the condition of cystadenoma of the bile-ducts, where such localized conditions have so been described, is merely an early and localized condition of the more advanced polycystic disease of the liver, and that probably Mr. Arthur Evans' case terminated in this way.

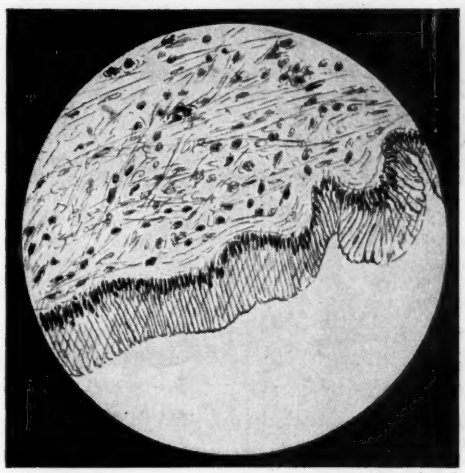


FIG. 151.—From Mr. Arthur Evans' case of cystadenoma of the bile-ducts. (*Brit. Jour. Surg.*, 1921, ix, 155. *C.R.* 17–476; *Section No.* 2308A.) No trace of liver substance is to be found in the sections; the walls of the cyst are rather more cellular than those of the others illustrated, but in parts the fibrous tissue is well formed. The cells are high narrow columnar, and the nuclei elongated in the same axis; but in many of the cysts of the other cases, columnar cells of mucus-secreting type are to be found, even when the bulk of them are, or have become, cuboidal or flat. Without questioning the origin from biliary duct cells, it is open to doubt whether the cystadenoma is derived from the fully-developed and functioning ducts of the adult liver to which the tumour was attached.

It is of interest to note that the patient from whom the 'solitary cyst' was removed had also another abnormality, in that the left kidney was shaped like two-thirds of a horse-shoe, and the ureter crossed the lower median pole, which extended beyond the middle line. This indicates some aberration in the differentiation of the Wolffian body, and will be seen to have some bearing on our final conclusions.

BRIEF NOTES ON OTHER RECORDED CASES OF POLYCYSTIC DISEASE OF THE PANCREAS, ETC.

Polycystic disease of the kidney has been observed in at least one case of cystadenoma of the pancreas, and since looking up the bibliography of

similar cases we have come across the figure illustrated in our *Fig.* 152, which is from a case of polycystic 'degeneration' of the spleen, of which condition a good example also is illustrated in Silvestrini's *Patologia e Chirurgia della Milza* (*Fig.* 153). The histological appearances could be matched exactly in any of our sections.

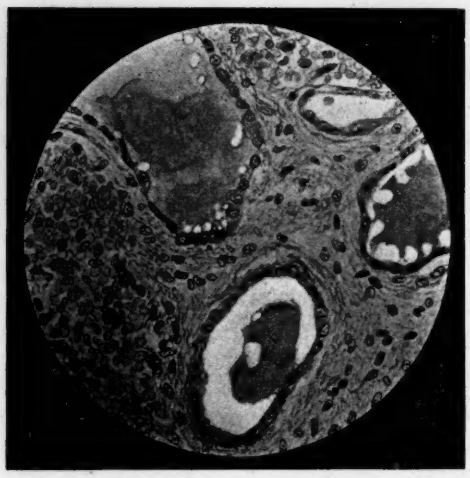


FIG. 152.—Section from a case of polycystic disease of the spleen. (Reproduced by the courtesy of Dr. E. H. Pool, from the *Surgery of the Spleen* by Eugene H. Pool and Ralph G. Stillman: Appleton, 1923.)

Practically the whole recent literature is to be found in Gross and Guleke's "Die Erkrankungen des Pankreas", 1924,[2] where there is a short account of cystadenomata, but no plate of microscopical appearances. One or two additional cases may be noticed briefly.

In Bolt's case,[3] in a female of 51 years, there was involvement of the whole pancreas, the cysts in the body and head being larger than those in the tail, the largest the size of a cherry-stone. The right kidney was in a condition of polycystic disease. The pancreatic tumour was reached through the lesser sac, as was ours; but unlike our *Case* 1, was "easily delivered". Clinically there was great emaciation, and the diagnosis was "cancer of the pylorus, with hepatic metastases". The functions of the pancreas were normal. Recovery occurred after the operation. The cells lining the cysts were of a columnar type. Malcolm's[4] first case was a female, age 50, who complained of loss of flesh, debility, and melæna. The urine was normal. A mobile tumour, 4 in. by 4 in., was situated in the left upper abdomen, and the clinical resemblance was to a malignant growth in the left kidney. In this case "some of the proper glandular tissue suggested that of the pancreas". "In some places there were masses of polyhedral cells, some of striking size

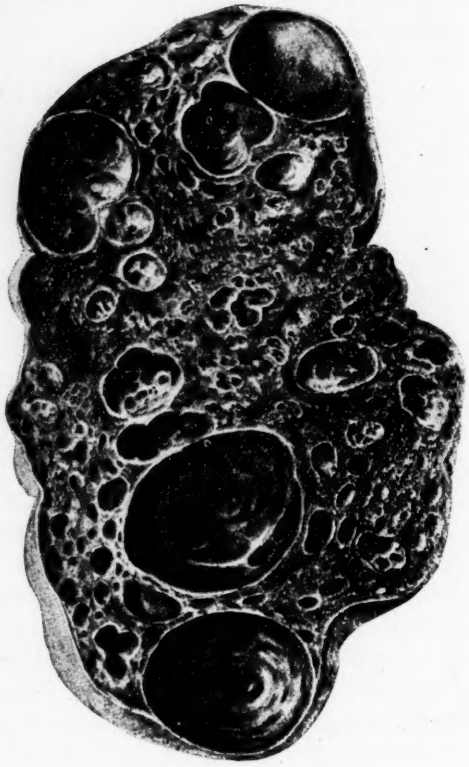


FIG. 153.—Polycystic spleen in section. (Reproduced by the courtesy of Professor Silvestrini, of Rimini, from *Patologia e Chirurgia della Milza*: Capelli, Bologna, 1924.)

and with more than a single nucleus." Malcolm's second case was a female of 49, in whom the tumour was thought to be a hydronephrosis of the left kidney. The cysts (two large and several smaller) contained blood, and a fluid that was amylolytic, but in this case there had clearly been rupture and access of pancreatic juice. Pitchford's case was easily shelled out, though it weighed over 2 lb., but the fluid showed no trace of pancreatic ferments. The cells present were polyhedral, with clear body and deeply-staining nuclei. The cysts were lined with short columnar cells.

CONCLUSIONS.

It seems to us that at least the more isolated of these cystic masses are embedded in the organ 'by accident', their cellular characteristics, whilst adenomatous in type, differing quite markedly from those of the organ in which they are found. Though it must be confessed we have not tested the ferment activity of the fluids in our cases, yet the cyst contents of the

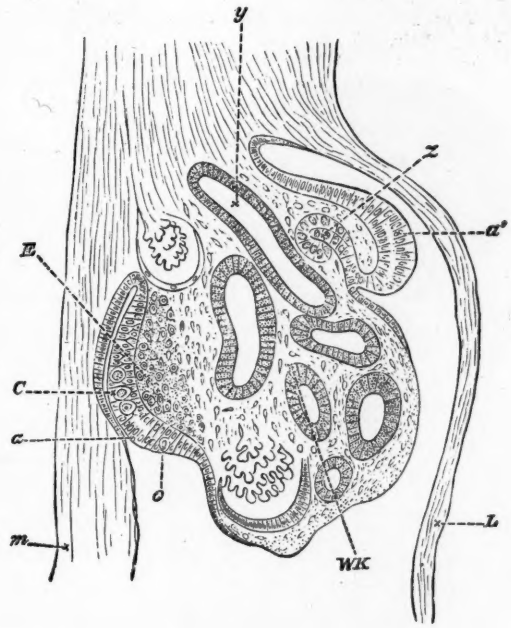


FIG. 154.—Section of the Wolffian body, developing pronephros, and genital gland of the fourth day. (× 160. After Waldeyer.)

m, Mesentery; *L*, Somatopleure; *a'*, Portion of the germinal epithelium from which the involution (*z*) to form the pronephros (anterior part of Müllerian duct) takes place; *a*, Thickened portion of the germinal epithelium in which the primitive germinal cells *C* and *o* are lying; *E*, Modified mesoblast which will form the stroma of the ovary; *WK*, Wolffian body; *y*, Wolffian duct.

(Reproduced by permission of Messrs. Macmillan & Co. Ltd., from Balfour's *Comparative Embryology*, Vol. II.)

pancreatic cases were of the same mucinous type as those we noted in the polycystic kidneys and in the liver, and there is no reason to suppose that they had any particular ferment action. We believe that it is not going too far to say that all these conditions can be brought into line and explained by assuming the inclusion of isolated portions of the Wolffian body either in the enteric buds forming the liver and pancreas in the embryonic spleen as it develops in the ventral mesogastrium, or of that part of the intermediate cell mass in which the kidney forms.

In the embryo these organs all arise in the immediate vicinity of the Wolffian body, and although it has been 'fashionable' for a long time to

dispute this theory of the origin of the polycystic condition of the kidneys, yet no one has really advanced a better one or one that will cover the whole ground, and it is in our opinion a reasonable suggestion that on this theory we can also explain these interesting and rare polycystic conditions of the pancreas, liver, and spleen. A reference to *Fig.* 154, reproduced from the diagram by Waldeyer given in *Quain*, 10th edition, vol. i, plate 1, p. 120, showing the embryo of the chick, gives, for example, the type of cell and structure found in these tumours.

REFERENCES.

[1] EVANS, ARTHUR, *Brit. Jour. Surg.*, 1921, ix, 155.
[2] GROSS and GULEKE, "Die Erkrankungen des Pankreas", *Enzyklopaedie der klin. Med.*, 254 (extensive bibliography).
[3] BOLT, R. F., *Ibid.*, 1913, i, 142.
[4] MALCOLM, *Clin. Soc. Trans.*, xxxix, 175 (short bibliography).

THE PATHOLOGY OF HYDRONEPHROSIS.

By H. P. WINSBURY WHITE, London.

(Being a Hunterian Lecture delivered at the Royal College of Surgeons of England on February 4, 1925.)

In spite of the voluminous literature which exists on the subject of hydronephrosis, there is still a widespread diversity of opinion as to the primary etiological factor in the pelvic type of the disease. This has been largely due to lack of opportunity in the past to study the earliest examples of the condition; and because investigations have been generally carried out on specimens in advanced stages of dilatation, cause and effect have been largely confused.

To hydronephrosis from such undisputed causes as calculus or growth involving any part of the urinary tract, or from any form of obstruction to the lowest urinary passage, I shall make no further reference, except to point out that the striking feature in the pathological anatomy when due to any of these causes is that the dilatation advances more markedly in the calices than in the pelvis. *Fig.* 155 illustrates this point. It is an advanced example of calculous pyonephrosis resulting from the small stone in the renal pelvis.

Fig. 155.—Renal type of hydronephrosis, resulting from stone in the pelvis of the kidney. (Lantern slide.)

When the obstruction is due primarily to a stenosis in the region of the pelvo-ureteral junction, the dilatation is more marked in the pelvis than in the calices. Hence the term 'pelvic hydronephrosis'. The result of this pelvic distention is an abrupt separation of pelvis from ureter. This definite demarcation between these two components of the efferent system is essentially a pathological one, for it is not possible in a healthy kidney to indicate accurately, either macroscopically or microscopically, the actual locality where the pelvis ends and the ureter begins.

I have been able to note details of 159 cases of hydronephrosis. A large number of these were from the literature, others were from the records of the Royal Free Hospital and from notes of my own personal cases. I have arranged these in *Table I* according to the chief features of their pathological anatomy as follows:—

Table I.—Classification of 159 Cases of Hydronephrosis according to Certain Pathological Features.

	No. of Cases
Pelvic hydronephrosis—	
Simple unilateral	121
Simple bilateral	2
Ectopic kidney—	
Unilateral	5
Horseshoe kidney—	
Unilateral	5
Bilateral	1
Double ureters—	
Unilateral	1
Bilateral	1
Dilated bladder, both ureters, and kidneys—	
Without apparent cause	3
Phimosis	1
Atresia of external urinary meatus	1
Dilatation of whole ureter and kidney—	
Unilateral	6
Bilateral	8
Dilatation of upper half of ureter and kidney—	
Unilateral	2
Traumatic hydronephrosis—	
Injury to ureter (verified) ..	2
Total ..	159

I have not discriminated between those in which there is a blood-vessel which is said to be compressing the ureter and those in which this is not apparent, for the reason that after division of the offending vessel the appearance of the two varieties does not differ, and there is no reason to believe that the etiology in the two cases is not the same. In each case it is a hydronephrosis with the dilatation beginning at the pelvo-ureteric junction. *Table I* shows that 85 per cent of the 159 cases were of this variety, and that more than 97 per cent of these were unilateral.

CONGENITAL HYDRONEPHROSIS AND HYDRONEPHROSIS IN CHILDREN.

The term 'congenital' has been freely used to describe not only those cases which occur in fœtal and in the early periods of independent existence, but also many cases which first attract attention at some period of adult life. Most of the earliest cases may be definitely accepted as congenital, for many are found in association with abnormalities of this nature involving other parts of the body, such as spina bifida and imperforate anus. Blackwood, in writing of 28 cases that he collected of hydronephrosis in infants, states that he found an associated congenital defect in 9. It is of some interest to note that heredity also plays a part, for the same writer refers to the reported case of a woman who gave birth to three premature children, each with a hydronephrosis.

Unlike the cases first noted in adult life, hydronephrosis in children is frequently accompanied by dilatation of the corresponding ureter. Of 32 cases in children under twelve years of age that I have noted from the literature, 17 had dilatation of one or both ureters, both being involved in 10 cases. In the remaining 15 cases the dilatation began at the pelvo-ureteric junction. The length of life when both ureters are dilated is generally short, most of the cases dying within the first two years of life. This fact was noted by Davis, who refers to a report of 25 cases of bilateral dilatation, nearly all of which were under ten years old.

With regard to the cause of the dilatation, in two only of the bilateral cases that I have collected was a definite obstruction to the outflow of urine from the penis described. In one instance this was a phimosis, in the other a narrow external urinary meatus. In a few cases constrictions at the vesical ends of both ureters were described as the cause. Several instances were met with in which the bladder as well as the ureters was dilated without apparent reason. It is important to recognize that dilatation of the bladder may be present when no urethral obstruction can be found. Bard has described 3 cases, all in males, at the ages of 16, 36, and 48 respectively. In several cases of unilateral dilatation of the ureter, a stricture at the junction of the ureter with the bladder was described. In others the cause was not indicated. It would be interesting to know whether dilatation of the bladder ever accompanies unilateral ureteric dilatation as a congenital condition. Poynton described the case of a boy, age 6, in whom the dilated left ureter was demonstrated in a cysto-ureterogram, but it was not ascertained whether the other ureter was not dilated to a lesser degree. Unilateral dilatation may escape recognition till puberty or later.

When the ureter is not involved in the dilatation there is always to be seen an abrupt demarcation which separates a distended pelvis from a narrow ureter. The impression from this is generally that the size of the ureteral lumen is inadequate as an efferent urinary duct. In some of the most striking fœtal and infantile cases described no lumen of the ureter existed at all.

The question of inadequacy of the ureter is one of very great interest, and was brought forward many years ago by Bland-Sutton as the chief cause of the type of hydronephrosis which begins at the pelvo-ureteric junction. That the condition occurs also in an acquired form as the result of chronic inflammation is certain from the evidence I have brought forward. Geraghty and Frontz in 1918 expressed the view that abnormalities in ureteral calibre are probably the most important factors in the production of hydronephrosis. When one recalls that cases occur which first give rise to symptoms during any year of childhood, adolescence, or adult life, it becomes extremely difficult to know where to draw the line between the congenital and the acquired disease. But the fact that the great majority of cases manifest their first signs of disease after the age of twenty speaks strongly in favour of these being acquired rather than congenital.

Such features as high or oblique insertion of the ureter into the pelvis, and contracted or valve-like pelvic outlet, often referred to as congenital, are seen only in advanced stages of hydronephrosis, and are a consequence

not the cause of the disease. These points are dealt with under inflammation.

REFERENCES.—12, 18, 23, 24, 25, 26, 29, 30, 31, 35, 36, 37, 40, 42, 46, 47, 48, 50, 51, 53, 57, 59, 69, 74, 76, 79, 84, 85, 86, 90, 94, 95, 100, 106, 109, 112, 116, 120, 122, 123, 124, 125, 129, 131, 132.

HYDRONEPHROSIS ACCOMPANYING CONGENITAL ABNORMALITIES OF THE KIDNEY.

It has been suggested that a congenital abnormality such as a horseshoe or an ectopic kidney predisposes to hydronephrosis. Papin says that hydronephrosis is a very frequent affection of horseshoe kidney. He gathered from the literature 14 such cases, and reported 13 others found at autopsy. It is not a question of the ureters being compressed between the transverse portion of renal tissue and the posterior abdominal wall, for in all cases but one the ureters passed in front of the renal tissue. He gives an illustration of a horseshoe kidney with both pelves dilated. Ectopic kidney is also frequently the seat of a hydronephrosis, and many cases are reported in the literature. The misplaced organ may lie either above or below the brim of the pelvis.

FIG. 156.—Pelvic type of hydronephrosis in a vertical pelvis.

In considering the shape of the renal pelvis as a predisposing cause. Bazy claims that the pelvic type of hydronephrosis results from a congenital peculiarity of the pelvis. He describes the pelves as intra-renal, extra-renal, and intermediate between these types, according to the relationship of the pelvis to the renal tissue. He considers that an extra-renal horizontally-placed pelvis, of the shape of the distended bag of the bagpipes (bassinet en cornemuse), is the predisposing element, and that this type of pelvis is only primitively developed. He says, however, that other varieties of pelves are capable of dilatation, but that a vertically-placed pelvis is not. In a large number of specimens representing various stages of the disease that I have been able to inspect I have not been able to recognize the bagpipe pelvis as a common feature. I disagree with the observation that a vertically-placed pelvis is never associated with a hydronephrosis. *Fig.* 156 is an excellent example of a hydronephrosis involving such a pelvis.

Double ureter is another congenital abnormality which frequently is complicated by hydronephrosis involving one portion of the divided drainage system. Papin calls attention to this fact. It is not usual for the dilatation to involve both portions of the division. It is said that the upper pelvis and its calices are more frequently involved in the dilatation than the lower. There are, nevertheless, records of many examples where the latter and

not the former is the seat of the disease. *Fig.* 157 is an illustration of this.

When the ureter is dilated as well as the pelvis, it is generally found that the exit of the dilated ureter opens in a situation other than the bladder, and has a narrowed orifice. The posterior urethra is perhaps the commonest locality in which this abnormal orifice is found; but it may open in many sites in the male or female genital organs, or into the rectum.

It is sometimes observed that the two ureters coming from the same kidney are spirally arranged one around the other throughout their course, the number of turns varying in different cases between one and three. It is claimed by some that these twists are the causal factor in the hydronephrosis. I can find no facts in the literature to support this view. On the contrary, many examples of the spiral arrangement have been noted without hydronephrosis. Papin gives an illustration of such a bilateral condition. He also illustrates several specimens of hydronephrosis in which the two ureters are not intertwined. It may be noted that a dilated ureter is by no means a constant feature of a hydronephrosis associated with this abnormality, for the distention frequently begins at the pelvo-ureteral junction, as is common in kidneys with other congenital abnormalities (*Fig.* 157).

FIG. 157.—Kidney with double ureter and pelvis, with hydronephrosis involving the lower pelvis and its calices. Note the kinking of the lower ureter.

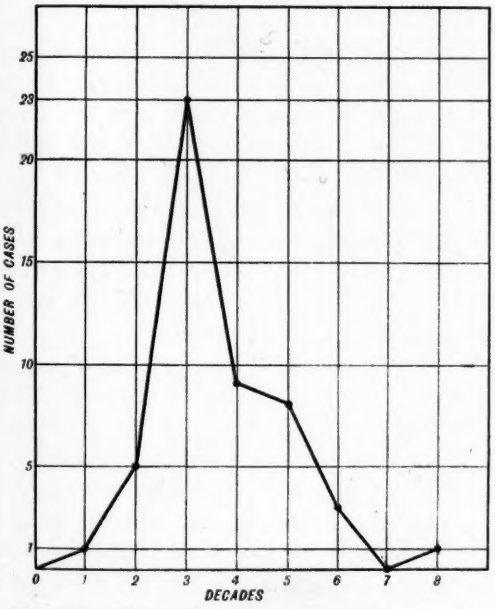


FIG. 158.—The age incidence expressed in decades in 50 cases of hydronephrosis.

REFERENCES.—7, 11, 12, 15, 17, 46, 50, 53, 60, 64, 76, 93, 95, 96, 102, 109, 110, 123, 130, 133, 136.

AGE AND SEX INCIDENCE AND SITE OF LESION.

The preponderance of the third decade of life as the period of onset of the disease is very striking. Braasch, in reporting on 116 cases from the Mayo Clinic, gives the average age as 21. The chart (*Fig.* 158), which sets

out the age incidence expressed in decades, of 50 cases shows that 23 of these manifested their first symptoms between the ages of 20 and 30. It is to be noted that the onset in one case was at the age of 75. From this it appears that hydronephrosis is a disease which may occur at any period of life.

In a further study of the same cases 33 were found in females and 17 in males. The left kidney was the seat of the disease in 26 instances, and the right in 24. There was no case of bilateral disease. Other writers have reported that hydronephrosis is twice as common in women as in men.

REFERENCES.—9, 15, 21, 25, 26, 29, 33, 36, 42, 43, 44, 46, 47, 50, 53, 54, 58, 59, 67, 68, 74, 76, 79, 81, 82, 86, 91, 100, 106, 107, 108, 109, 116, 117, 119, 123, 124, 125, 128, 130, 131, 132, 133.

INFLAMMATION AS A CAUSE OF HYDRONEPHROSIS.

From the point of view of establishing the primary etiological factor of hydronephrosis, it is on the earliest cases that observations may be considered of greatest importance. It is, however, only as a result of ureteric catheterization and pyelography that one is able to detect with certainty, and thus has an opportunity to study, the disease in its incipient stage. *Figs.* 159, 161–163 all show specimens of the disease which is still early. It is important to study these examples to search for a common feature which would account for the phenomenon of pelvic dilatation.

FIG. 159.—An early specimen of hydronephrosis. (Lantern slide.)

Fig. 159 is the earliest case of which I have had personal experience. It is the right kidney of a man, age 29, who suffered from attacks of pain in the right side over a period of three years. The attacks at first occurred at three-monthly intervals, but the periods between the attacks gradually shortened until eventually they took place as often as once a week.

The pain suffered by these early cases is often extremely severe. The explanation of this is quite apparent on examining a section of the pelvis under the microscope, for a considerable degree of muscular hypertrophy can be made out. So early a stage of dilatation is represented in the specimen we are considering, that, when handling the organ at operation, it was not at all certain from its appearance that it had been the seat of a general dilatation, so little change was there to be seen in its contour. However, in the knowledge of the pyelographic appearance of this kidney (*Fig.* 160), I had no hesitation in treating it as a hydronephrosis.

Fig. 161 is also a very early stage of the disease. It is the right kidney of a male, age 28, who had attacks of pain in the right side for eight months. *Fig* 162 is a slightly further stage of dilatation than is shown in either of the

two foregoing specimens. It is the left kidney of a boy, age 15, who had had an operation for acute appendicitis at the age of 13, and who had suffered from intermittent attacks of pain in the left side since.

Fig. 163 is the left kidney of a woman, age 40, who had suffered from attacks of pain in the left side for three and a half years. Nephropexy was carried out soon after the onset, with temporary relief. Marked thickening of the ureter is obvious in this specimen, and was in fact strikingly present

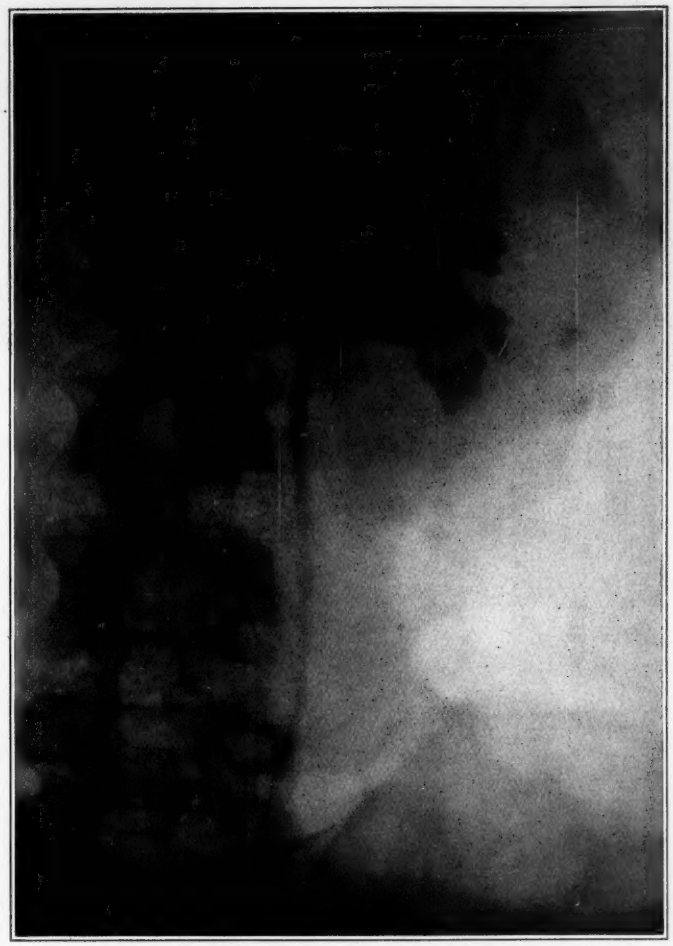


FIG. 160.—Pyelogram of the kidney represented in *Fig.* 159.

in the attached portions of the ureters in all the specimens just discussed. Microscopically this change can be seen to be due to an accumulation of fibrous tissue in the mucous coat (*Fig.* 164). The fibrous tissue has given rise to a definite narrowing of the lumen and is the result of a past infection in the wall of the ureter. The section is from the very early case represented in *Fig.* 165.

The ureters of 14 other specimens showed just the same kind of

FIG. 161.—Another early specimen of hydronephrosis. The dilatation is first noted in the pelves of these early examples.

FIG. 162.—Early hydronephrosis, but slightly more advanced than in the two foregoing examples.

FIG. 163.—Early hydronephrosis, showing very marked thickening of the ureter from inflammation. (Lantern slide.)

change, but in different degrees. One cannot, however, bring forward advanced cases of hydronephrosis, and point to the marked inflammatory changes in the ureter, and maintain that these must be the cause of the hydronephrosis, for it may be said in such instances that the inflammation of the pelvis and ureter is a consequence and not a cause of the dilatation. It is not possible to prove which is the case by investigating the grosser examples of the disease, but the presence of old-standing inflammatory change in the ureters and pelves of the earliest specimens of hydronephrosis strongly suggests that the inflammation is of longer standing than the dilatation. This is the only way to account for a long history of attacks of pain which is sometimes a puzzling feature of cases that are obviously extremely early,

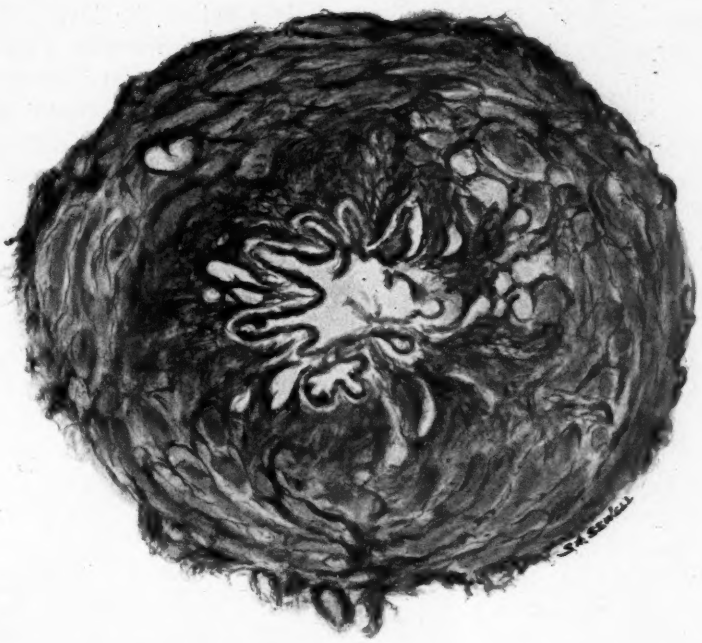


FIG. 164.—Low-power transverse section of upper end of ureter, from specimen shown in *Fig.* 159. Note the marked fibrotic change in the submucous region, and that this has given rise to constriction of the lumen.

judging from the amount of dilatation. The explanation is that the symptoms at first were due to chronic pyelitis, and later to hydronephrosis or to both of these causes. Take the case represented by *Figs.* 159 and 164. On naked-eye examination it is about as early a stage of dilatation as one is able to recognize, and yet the patient had suffered from his attacks over a period of three years. The microscopic section of the ureter leaves no doubt about the chronicity of the inflammatory change. Geraghty and Frontz, in a detailed examination of the upper end of the ureter in 9 cases of hydronephrosis, found definite narrowing of the lumen in all. In 8 they considered that chronic inflammation was the cause, and in the remaining case hypertrophy of muscle about the pelvic outlet.

In all of the above specimens that I have brought forward it is to be noted that there is a complete absence of any kinking or angulation of the upper end of the ureter. This change, on the other hand, is a common feature of advanced examples of hydronephrosis. It is due to one or both of two causes—namely, an implication of the upper end of the ureter by a renal blood-vessel during the process of pelvic distention, and a sagging of the pelvis below the level of the point at which the ureter joins the peritoneum, for the latter structure gives a certain amount of fixation to the former. The distorted course of the ureter in some of the more

FIG. 165. — Fairly advanced hydronephrosis, showing pelvis and ureter in contact. (Lantern slide.)

advanced cases can often be clearly seen in pyelograms with an opaque ureteric catheter in position. One result of the pelvic sagging is that the pelvis and a certain length of the ureter are brought into intimate contact (*Fig.* 165). This contact is maintained by the formation of adhesions resulting from the spread of inflammation which is present in the ureter and pelvis in all cases. The oblique course thus given to the ureter adds another obstructive process to the pelvic outlet, which becomes oblique and valve-like; further pelvic distention and sagging occur, so that eventually the

FIG. 166.—Posterior view of a left hydronephrosis. The ureter has become looped over the abnormal venous tributary to the spermatic vein shown in *Fig.* 177.

ureteric orifice, instead of being at the most dependent point of the pelvis, may be found half-way up or higher on the pelvic wall. Many specimens of the most advanced stages of hydronephrosis show the multiplicity of obstructive processes to the urinary outflow from the pelvis that I have just described. Each of these is often quoted singly as the cause of hydronephrosis.

In the most advanced specimen of the disease which I have been able to investigate in detail the following facts were all to be noted: (1) Looping of the ureter over a blood-vessel (*Fig.* 166); (2) Adhesions between pelvis and ureter, with marked obliquity of the upper part of the latter; (3) A contracted valve-like pelvic outlet; (4) Marked inflammatory change in the ureter, with shrinking of the whole of this structure and narrowing of its lumen (*Fig.* 170 D). The extent to which the lumen is narrowed is sometimes best appreciated by inspecting the pelvic outlet, and seeing how stenosed this has become.

FIG. 167. — Hydronephrosis, showing acute pyelitis and thickening of ureter from chronic inflammation.

It is hardly possible that the inflammatory changes described as being constantly present in the ureters of hydronephroses are not present in the pelves as well. Of the 18 specimens which I have examined microscopically none failed to show these. There was to be seen in each an accumulation of fibrous tissue, in the mucous region extending often into the muscular coat, and infiltrated with varying numbers of inflammatory cells.

Fig. 167 is a good example of pyelitis in association with hydronephrosis. The injected areas of the pelvis, situated mostly round the orifices of the minor calices, indicate the regions of most active inflammation. The thickening of the pelvis and ureter—especially at the junction of these two structures—indicates how chronic the condition has been.

It is convenient at this stage to study the series of changes in the ureter when it is the seat of chronic inflammation in association with pyelitis. In the first place there is a general hypertrophy of all the coats, accompanied by a dilatation of the lumen and lengthening of the whole ureter. This is followed by a gradual accumulation of fibrous tissue, commencing in the mucous coat and gradually extending more deeply, so that the ureter becomes

considerably thickened and still has a dilated lumen. Ultimately, as the mass of fibrous tissue contracts, the whole ureter shrinks and the lumen is seriously constricted. Each of these stages is seen during the progress of renal tuberculosis.* The first two stages are met with more commonly than the last, because the majority of tuberculous kidneys are removed before the last stage is reached. *Fig.* 168 illustrates these three stages. In the last example the kidney has been completely destroyed by the tuberculous process, and the ureter reduced to a solid mass of fibrous tissue, so that the lumen could only be made out under the microscope. The dilatation of the ureter which occurs is quite independent of any obstruction to the lower part of the duct. Braasch, Rafin, and Boeckel all call attention to the above-mentioned changes in tuberculous ureteritis. The changes in the ureter corresponding to those of tuberculous disease are equally evident in chronic infection due to causes other than tuberculosis.

FIG. 168.—Three specimens of tuberculous kidneys, illustrating the three stages of chronic inflammatory change in the ureter. A, Dilatation; B, Thickening; C, Contraction.

The dilatation of the pelvis, and dilatation and elongation of the ureter, associated with early chronic *Bacillus coli* pyelitis are easily and frequently shown by pyelo-ureterogram, the redundancy of the ureter showing itself as a fold at the upper end.

* I had a recent clinical experience of the dilatation and patency of a tuberculous ureter. After passing a ureteric catheter up to the pelvis of a tuberculous left kidney, the catheter was seen to move regularly up and down the ureter, the oscillations synchronizing with the respiratory movements of the patient.

Dilatation of the ureter is commonly found accompanying the early stage of renal calculus. *Fig.* 169 represents cross-sections of various ureters, drawn to scale, illustrating the changes due to chronic inflammation. The first is a normal ureter, the second is from a case of renal calculus. A stone the size of a filbert nut lay in the renal pelvis, and gave rise to a slight degree of

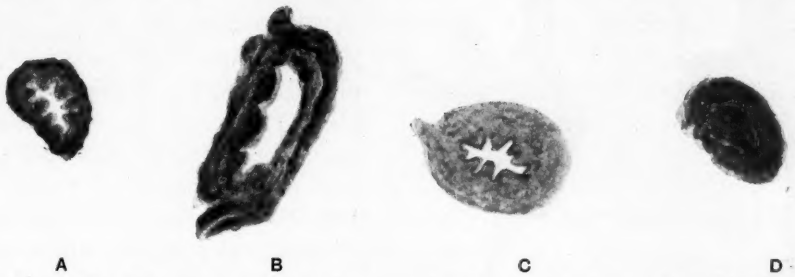


FIG. 169.—Transverse sections of ureters showing changes due to chronic inflammation. A, Normal ureter; B, Ureter of chronic pyelitis; C, Ureter from calculous pyonephrosis; D, Ureter from advanced renal tuberculosis.

chronic pyelitis. The whole ureter is hypertrophied and the lumen dilated. The third section is from a calculous pyonephrosis. The kidney substance had been completely destroyed. The wall of the ureter is considerably thickened by infiltration with chronic inflammatory tissue, and the lumen is somewhat narrowed. The fourth is from an advanced case of renal tuberculosis. The kidney had been completely destroyed and no lumen could be made

FIG. 170.—Transverse sections of ureters from specimens of hydronephrosis, showing shrinkage of ureter and narrowing of lumen as the disease advances.

out on naked-eye inspection of the ureter. These same changes are to be found in the ureters of pelvic hydronephroses. *Fig.* 170 is a series representing these. A is a normal ureter and D is from a more advanced stage of hydronephrosis than either of the two foregoing.

In regarding the whole series, not only does the lumen become progressively smaller, but the ureter shrinks as the disease advances. This reduction in size of the ureter as a whole is a common feature of old-standing cases of hydronephrosis, and results in a general inadequacy of the lumen.

REFERENCES.—19, 23, 24, 28, 32, 50, 53, 61, 111, 118.

EXPERIMENTAL DEMONSTRATION AND CLINICAL INVESTIGATION OF STRICTURE OF THE URETER.

I have been able to demonstrate experimentally the presence of inflammatory strictures in the upper ends of ureters which macroscopically appeared to be perfectly healthy. The method adopted was to take a freshly

removed post-mortem kidney and ureter of an adult and to inject hot jelly through the divided end of the ureter until the kidney and pelvis reached the limit of their capacity for distention. The whole was then allowed to solidify and fixed in formalin.

In this way 25 kidneys were examined. In 4 there appeared, as the distention reached its limit, a stricture in the region of the pelvo-ureteric junction (*Fig.* 171). In the remainder no such constriction appeared; *Fig.* 172 shows some of these. *Fig.* 171 reveals clearly four examples of narrowing of the upper end of the ureter. In B and D the narrowing is considerable in both the transverse and long axis of each ureter. A and C show more localized and less marked constrictions. Sections of these specimens through the strictured areas show that the stenosis is due to an accumulation of well-formed fibrous tissue situated in the mucous coat. There was no discernible evidence of any recent active inflammation in any of the regions under investigation, but the appearance indicated in each case the scar tissue of a past inflammatory focus. The presence of these strictures in some cases, and their absence in others, indicates their abnormality.

FIG. 171.—Experimental specimens illustrating strictures in the vicinity of the pelvo-ureteral junction.

FIG. 172. — Experimental specimens illustrating the absence of strictures demonstrated in the preceding illustration.

The identification of ureteral strictures at various points along the course of the ureter by means of ureterograms is often quite unreliable, for what appears to be a stricture on one occasion may have completely disappeared at a subsequent examination carried out soon after. Hunner claims to have identified ureteral strictures by means of wax-tipped bougies. Walther has called attention to cases of ureteral stricture associated with calculus in the ureter. Out of 16 cases of such strictures, 9 had previously passed stones.

The site and nature of ureteral stenoses can only be studied accurately by investigations carried out at operations and on specimens of morbid anatomy.

REFERENCES.—34, 67, 129.

PYELITIS OF PREGNANCY AND OTHER INFLAMMATORY DISEASES AS PREDISPOSING CAUSES.

In view of the important rôle ascribed to inflammation in the etiology of hydronephrosis, a consideration of the evidence indicating any well-marked inflammatory disease occurring previously to the onset of renal symptoms is worthy of some attention. In examining the records of the cases I have collected from the files of the Royal Free Hospital and those I have personally observed elsewhere, I have found 37 cases in which the state of health previous to the commencement of renal symptoms was ascertained. In 32 (86·4 per cent) there was definite evidence of pre-existing chronic inflammation, or some severe acute infection. In 12 cases (35·2 per cent) gastro-intestinal disturbance was the antecedent. In 8 of these the disease was chronic, while in 4 there had been acute appendicitis. In 7 other cases the renal symptoms suggesting pyelitis had their first onset either during or following pregnancy. In 4 cases rheumatic fever had preceded the hydronephrosis. Pneumonia, pulmonary tuberculosis, typhoid, and malaria were noted among the other less common previous illnesses.

The incidence of gastro-intestinal disorders either preceding or accompanying pyelitis raises the question of the route by which the infection reaches the kidney from the intestinal tract. The frequent occurrence both of pyelitis and hydronephrosis as a unilateral disease suggests that the infection takes place by a lymphatic route rather than through the blood-stream. The lymphatic connection between the ileocæcal region and the right kidney is an important one in consideration of the frequent evidence we have of pyelitis complicating acute appendicitis. Hæmaturia as an accompaniment of acute appendicitis is by no means rare, and many cases have been reported. Block holds that the adhesions which are to be found about the pelvis of the kidney following acute appendicitis, by giving rise to obstruction of the ureter, lead to pyelitis, but it is far more likely that the adhesions owe their origin to the spread of inflammation from the pelvis and ureter, the infection of which structures is secondary to the appendicitis. This view is supported by finding the strongest adhesions adjacent to the pelvis and ureter.

It is doubtful whether a peri-ureteritis alone would cause sufficient scar tissue to constrict the ureter. The writer carried out on rabbits two experiments in which 10 per cent iodine was injected retroperitoneally round one

ureter. The animals were killed at nine and twelve months respectively following the experiments. Although considerable scar tissue had formed round each ureter concerned, no constriction leading to hydronephrosis resulted. It has to be borne in mind that while the ureter remains attached to the peritoneum the scar tissue cannot completely surround it, and thus cannot press it from all sides.

REFERENCES.—3, 5, 8, 10, 15, 19, 44, 50, 54, 62, 81, 99, 104, 114, 117, 133.

PYELITIS, INCREASED FREQUENCY OF MICTURITION, AND POLYURIA.

The association of pyelitis with hydronephrosis has escaped recognition largely because pyelitis is looked upon as a disease which is always associated with pus and bacteria in the urine and with increased frequency of micturition. From my own observations I am of the opinion that the milder degrees of the chronic form of the disease exist with only the scantiest pus and bacterial cells in the urine, and with these absent at certain periods. There is no reason why the inflammation should always go on to the stage of pus formation in this situation more than in any other part of the body. Exacerbations of the existing pyelitis will explain the attacks of pain which come on without apparent cause, and which are a striking feature of nearly all cases of hydronephrosis.

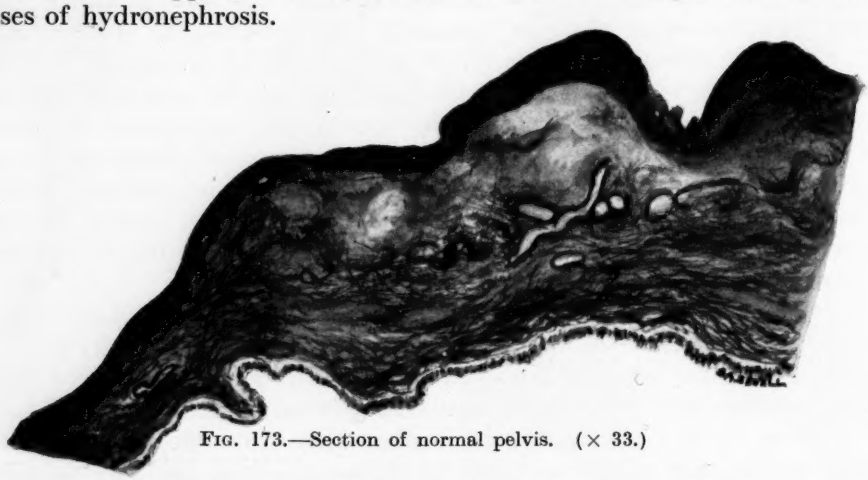


FIG. 173.—Section of normal pelvis. (× 33.)

Microscopic examination of the pelvis of eighteen examples of hydronephrosis shows that pyelitis is constant in this disease. *Figs.* 173, 174, 175 are sections under the low power of three renal pelves. The first is a normal one, the other two are early cases of hydronephrosis. In the hydronephrosis specimens the muscular tunics are highly developed, and there is a considerable accumulation of fibrous tissue in the mucous and submucous regions. The epithelium in the middle section is in a state of hypertrophy. In the same section the chronic inflammatory tissue has accumulated to such an extent as to give rise to a papilliform process. In the last section the signs of chronic inflammation are not so marked; on the other hand, there is a general infiltration by inflammatory cells, indicating a more acute process than in the former.

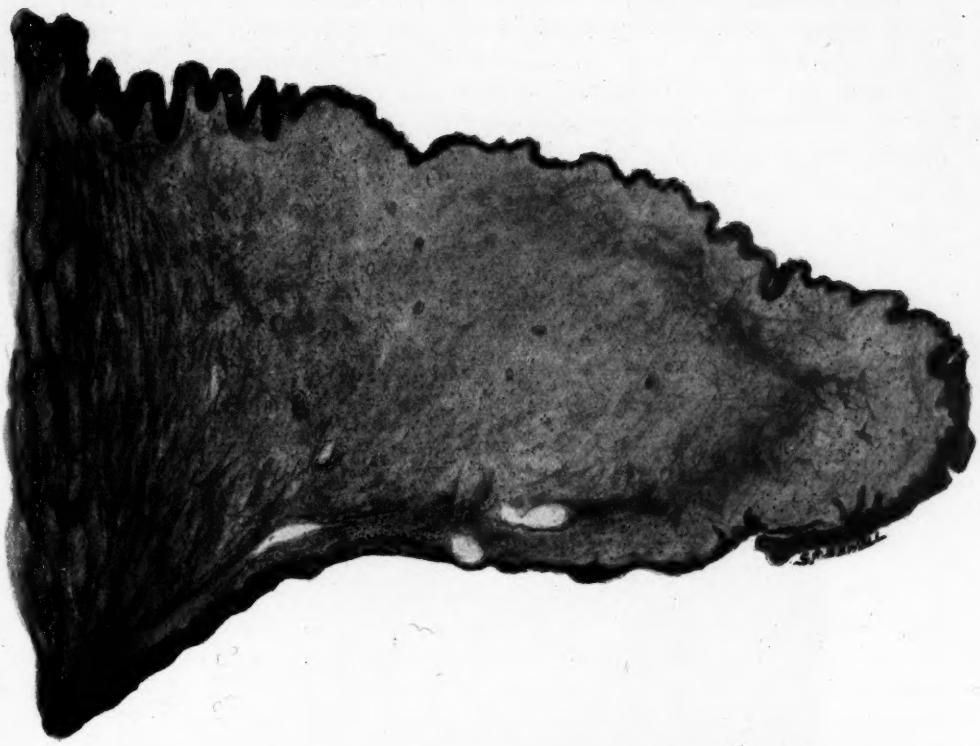


FIG. 174.—Section of pelvis of an early hydronephrosis. The chronic inflammatory tissue beneath the mucosa has formed a papilliform process. (× 33.)

FIG. 175.—Section of pelvis of an early hydronephrosis, showing a less degree of the same change as seen in the preceding section. (× 33.)

It is of some interest to compare the clinical features of these two cases. *Fig.* 174 is from a left hydronephrosis in a girl, age 16, who had had pain in the left side for four years. Several examinations of the urine had failed to reveal any bacteria. On one occasion a few pus cells were found. The patient had never suffered from any abnormal frequency of micturition, but on two occasions cystoscopy had revealed slight redness and swelling of the corresponding ureteric orifice. So that in this case with very marked pyelitis the association of inflammation with the hydronephrosis could only be definitely established by cystoscopy. Even this means may fail to reveal any signs of

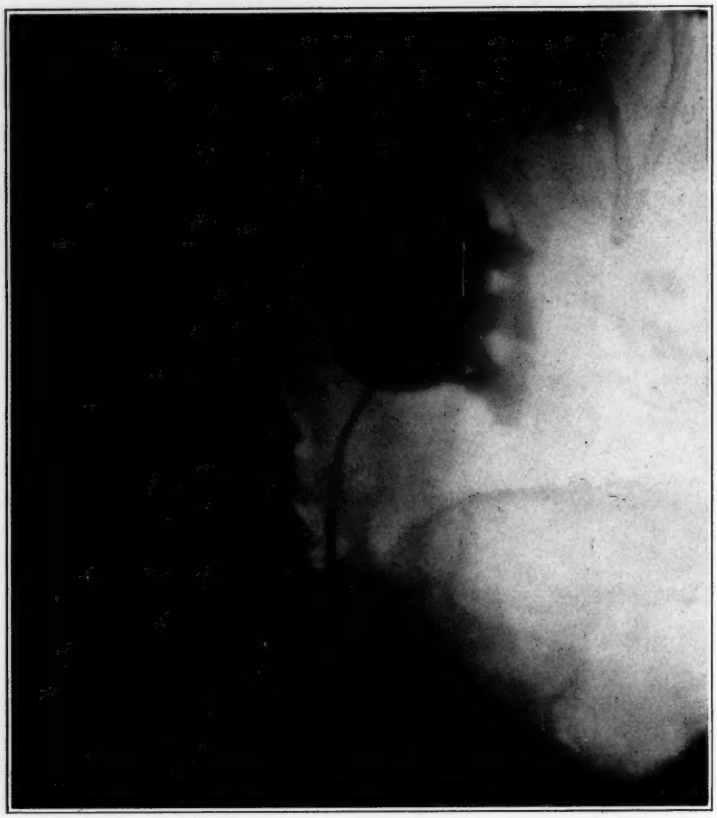


FIG. 176.—Pyelogram of early hydronephrosis.

inflammation if the examination is not carried out either during or soon after an attack of pain.

The clinical features manifested by the case represented by *Fig.* 175 were much more straightforward. The patient, a woman, age 43, suffered from attacks of pain in the right side and frequency of micturition over a period of six months. Several examinations of the urine all revealed considerable pus cells and *B. coli* in the urine. The greater abundance of inflammatory cells in the section of this pelvis is in keeping with the urinary symptoms and findings in this example. *Fig.* 176 is a pyelogram of the kidney, and shows

how early and yet how definite the hydronephrosis is. Block calls attention to the association of pyelitis with hydronephrosis, in quoting a number of personal cases.

From a consideration of the two foregoing cases it is apparent that any increase in the frequency of micturition is dependent on the acuteness of the pyelitis. Of 22 cases of hydronephrosis of which I have had personal experience, 50 per cent suffered from increased frequency in some degree, during the periods of the attacks.

Polyuria.—It is a common belief that a crisis of hydronephrosis culminates in a discharge of a large quantity of urine from the affected kidney, leading to frequency of micturition from the passage of a considerable measure per urethram within a very short period. This phenomenon, however, is only occasionally to be observed. The number of cases in which polyuria has been definitely established are surprisingly few. One has to bear in mind that there is a danger of misinterpreting the increased frequency and polyuria of pyelitis, which are often present in hydronephrosis. In the records of the numerous cases I have referred to, I can find only 5 instances in which polyuria was satisfactorily established. In the 22 cases of my own personal experience, I could find no evidence that this had occurred.

Polyuria, however, following a renal crisis, is well known to occur in kidneys in which it has been determined by operation that the organ is not the seat of a hydronephrosis. Albarran recorded 3 such cases. In one the attacks had been recurring for four years, and the patient would pass 1½ litres in three micturitions during an hour. At operation the kidney was enlarged from congestion, but there was no dilatation of the pelvis. He has observed hæmaturia in 3 cases of this kind.

That polyuria associated with hydronephrosis is due to just the same cause—namely, the relief of a congestion of a kidney—has been proved by the reports of many observers. These have agreed that the enlargement of the kidney which takes place is due to intense congestion, and that the size of the organ is frequently such that it could not possibly contain the amount of urine voided. Gardner records that a ureteric catheter passed during an attack has revealed not more than an ounce of urine in the pelvis, while Bazy has measured as much as 7 litres of urine in twenty-four hours from a similar case in which there was no pelvic dilatation.

Seeing that pyelitis has been definitely established as an accompaniment of hydronephrosis, there is every reason to believe that the renal congestion which occurs results from the attack of inflammation, which probably reaches its maximum in the wall of the pelvis, but which involves the parenchyma as well.

In reviewing the phenomena that I have described which are known to accompany a renal crisis, especially in a hydronephrotic kidney, it is clear that the congestion and enlargement of the kidney, the presence of redness round the ureteric orifice, and the increased frequency of micturition, all combine to suggest renal infection, even though pus and bacterial cells may be scanty and difficult to detect in the urine. The presence or absence of one or more of the signs or symptoms will depend on the degree of infection. In view of the constant evidence of nephritis, pyelitis, and ureteritis as revealed

by the microscope in these cases, it is impossible not to consider most seriously infection as the cause which precipitates an attack.

REFERENCES.—2, 3, 5, 17, 19, 21, 22, 23, 33, 44, 50, 52, 53, 54, 60, 65, 66, 75, 77, 79, 91, 128, 133.

RENAL MOBILITY.

Following the writings of Landau, of Terrier and Baudouin, and of Tuffier, renal mobility as the cause of hydronephrosis was for many years accepted without question. The events which were supposed to form the cycle leading up to a crisis seemed so obvious as to render criticism superfluous. Gradually, however, successive facts have been brought forward which have combined to show up fallacies in the old arguments, with the result that the theory of renal mobility as a cause of hydronephrosis has been almost completely discarded. I can find no record of any painstaking observations carried out by a modern investigator which does not discredit the theory of mobile kidney.

Briefly the events of the cycle credited to this theory are as follows: Owing to the mobility of the kidney the upper part of the ureter becomes kinked; this causes a retention of urine in the renal pelvis, with resulting pain and enlargement of the organ; subsequently the obstruction is overcome, when the discharge of a large amount of urine occurs, with relief of pain and diminution in size of the kidney. At first sight this explanation seems extremely reasonable, and one does not wonder that it was so readily accepted. However, the consensus of opinion now is that kinking of the ureter, to produce obstruction, must be long-continued, and that to bring this about fixation of the upper end of the ureter is an essential. But as the ureter is a flexible and elastic tube, kinking does not diminish the size of the lumen. Experimentally it has been shown that an acute bend in the ureter as a result of suturing together its walls does not produce a change in the renal pelvis. In post-mortem observations on the kidney I have been impressed with what appears to be the impossibility of producing an acute bend in the ureter, even after freely mobilizing the kidney as it lies *in situ*.

There is, however, no doubt that renal mobility is commonly found in association with hydronephrosis. The abnormal range of movement is, of course, a consequence of the hydronephrosis and not the cause of it. The variations in size of the organ give rise to a stretching of the fibrous sheath of the fatty capsule and of the vascular pedicle which runs across the front of the dilated pelvis.

Tuffier, in his experiments on dogs in which he attempted to cause hydronephrosis by mobilizing the kidney, could only kink the ureter by passing a thread round it. Legueu, Hildebrand, and Haga all demonstrated that the upper ureter must be fixed in order to produce obstruction by kinking this structure. Numerous cases of mobile kidney have been operated upon in which neither kinking of the ureter nor dilatation of the pelvis was to be made out, and many others have been investigated by ureteric catheterization and pyelography with the same result.

Fig. 157 makes an interesting study. There is a hydronephrosis involving the lower pelvis and its calices of a kidney with a double ureter. The kinking

of the commencement of the lower ureter is quite obvious. If it is to be assumed that this is due to a dropping of the whole organ from mobility, the upper ureter should be equally affected. The most acceptable explanation is that the redundancy of the ureter which has occurred in the early stage of inflammation, and the dilatation of the pelvis which has taken place later, have allowed these two structures to come into contact.

Henry Morris, in giving an account of 142 cases of hydronephrosis, is reported as saying: "I am much disposed to think that in several cases in which hydronephrosis and movable kidney coexist, the mobility was acquired after and not before the hydronephrosis".

The Dietl's crises sometimes to be observed in cases of movable kidney are no doubt due to renal retention, not from an obstructed outlet of the pelvis, but from a congested kidney resulting from a pyelitis consequent on chronic intestinal trouble so often present with general visceroptosis, of which the nephroptosis is a part. Many cases having long histories of crises fail to show any indication of a dilated pelvis when submitted to operation. Tuffier, in describing the results of 45 nephropexies for attacks of pain, could find no evidence of dilatation in 36. Geraghty and Frontz quote the combined figures of seven authorities, giving a total of 4576 cases. These show that mobile kidney occurs in 20 per cent of women and in 2 per cent of men. They also refer to Kelly and Burnham on 245 cases. They found the mobile organ on the right side in 177 cases, on the left in 25, and on both in 43. The writers go on to point out that if mobile kidney were the cause of hydronephrosis, we should find an overwhelming majority in women, right hydronephrosis more common than left, and double more common than left. None of these facts, however, is found to be the case, for the disease is but twice as common in women as in men, it occurs with equal frequency in either kidney, and the bilateral disease is rare. Moreover, mobile kidney is a condition with a marked preponderance of its incidence in the fourth decade, while it is during the third decade of life that most cases of hydronephrosis occur.

References.—17, 39, 43, 45, 50, 53, 77, 79, 81, 120, 124, 127.

TRAUMATISM AND HYDRONEPHROSIS.

The relationship of traumatism to the kidney or ureter in connection with hydronephrosis has been given positions of widely varying importance according to the views of different writers, but in reading the accounts of the majority of cases reported as traumatic hydronephroses it is seen that the diagnosis is reached merely on the detection of a cystic swelling in one kidney region, in a number of cases not many days after the receipt of injury. In some, repeated aspirations have sufficed to cure the condition.

In order to understand the position clearly it is essential to have an accurate knowledge of the pathological anatomy commonly seen in injured kidneys. Transverse fissures in varying numbers and extent, running from the hilum to the outer border, with the maximum width of the fissure at the hilum, is the commonest characteristic. It is frequently found that a fissure has involved the pelvis as well. Guterbock reported a torn pelvis in 40 per cent of 32 examples of injured kidneys found at autopsy. There are probably

many instances of one or more of the larger calices being opened in others. Thus urine will be extravasated into the perirenal capsule in such cases, and soon this sac will become a large cystic swelling. It is said of some of the earliest cases that the ureter becomes blocked with clot, and thus the kidney becomes distended. A knowledge of the results of experimental obstruction to the ureter shows clearly that the capacity of the kidney to become dilated into an enormous cyst within a few weeks or a much shorter time does not exist. From studies made on specimens of intermittent hydronephrosis, and with a knowledge of the clinical history of such cases, it is clear that only after obstruction has existed for a considerable lapse of time does the renal sac become distended to hold more than a pint of fluid. Nevertheless one frequently comes across examples in the literature of such cases as the following, which is put forward as a traumatic hydronephrosis: Two and a half months after injury to the left side, 6 quarts of fluid were evacuated by incision, from the left renal region of a man, age 44. No description of the pathological anatomy of the region was given. Similar cases are numerous.

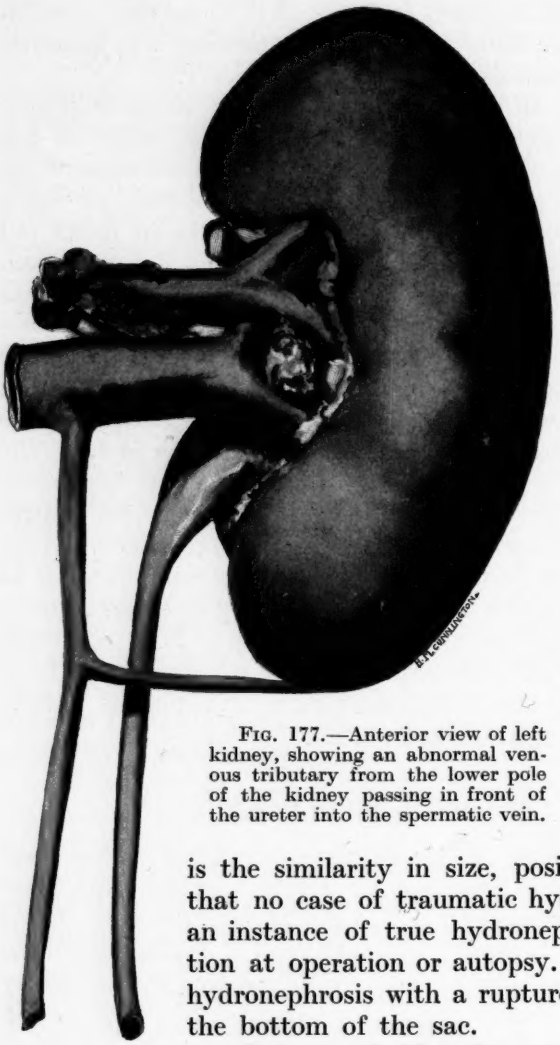


FIG. 177.—Anterior view of left kidney, showing an abnormal venous tributary from the lower pole of the kidney passing in front of the ureter into the spermatic vein.

Cabot says that so close is the similarity in size, position, consistency, and mobility that no case of traumatic hydronephrosis can be accepted as an instance of true hydronephrosis unless proved by dissection at operation or autopsy. He describes a case of pseudo-hydronephrosis with a ruptured and collapsed kidney lying at the bottom of the sac.

It is certain that for a true traumatic hydronephrosis to occur, an injury to the ureter is necessary. Dilatation of the kidney will take place only after the formation and contraction of scar tissue in the wall of the ureter. Should the injury be so severe as to cause a complete rupture of the ureter, there will result a peri-ureteral urinary cyst.

Amongst numerous cases reported as traumatic hydronephroses which I have looked up, in two only was the pathological anatomy properly investigated and the lesion of the ureter identified. One was that of a woman, age

26, in whom the lumen of the ureter concerned was completely obliterated by scar tissue two months after receipt of injury. The other was that of a man who was struck in one lumbar region by a piece of shell, and in whom ten years later a stricture of the ureter was identified as the cause of a hydronephrosis, which was then palpable.

One writer assumes that trauma is a common factor in the causation of intermittent hydronephrosis, and depends upon the fact that injury to the nephrocolic ligament allows nephroptosis to occur. This view, however, is not supported by any facts of pathological anatomy, but the writer quotes 7 cases out of 18 hydronephroses with a previous history of trauma.

REFERENCES.—8, 49, 50, 63, 71, 75, 80, 125, 127.

NORMAL AND ABNORMAL RENAL VESSELS IN RELATION TO HYDRONEPHROSIS.

A vascular complication of a hydronephrosis wherein the ureter is obstructed by a blood-vessel is of not infrequent occurrence. There are two sharply opposite points of view with regard to the rôle which these blood-vessels play. I have studied this complication in 11 examples illustrating the condition. These examples

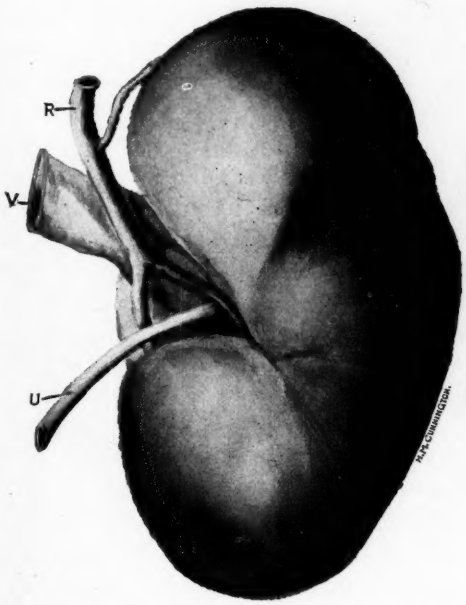


FIG. 178.—Posterior view of a right kidney, showing the normal inferior branch of the renal artery crossing in front of the upper end of the ureter. R, Renal artery; V, Vein; U, Ureter.

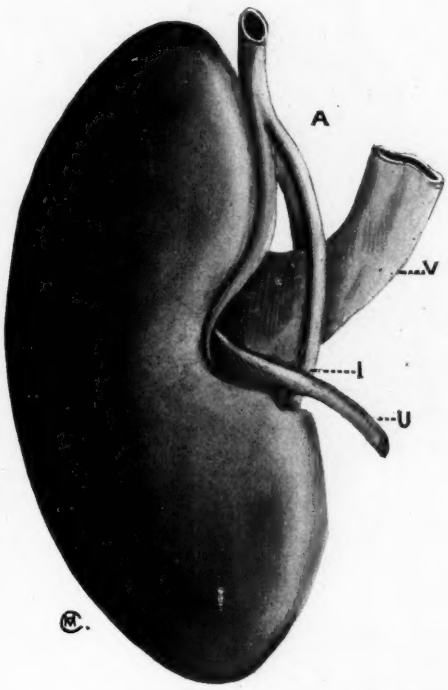
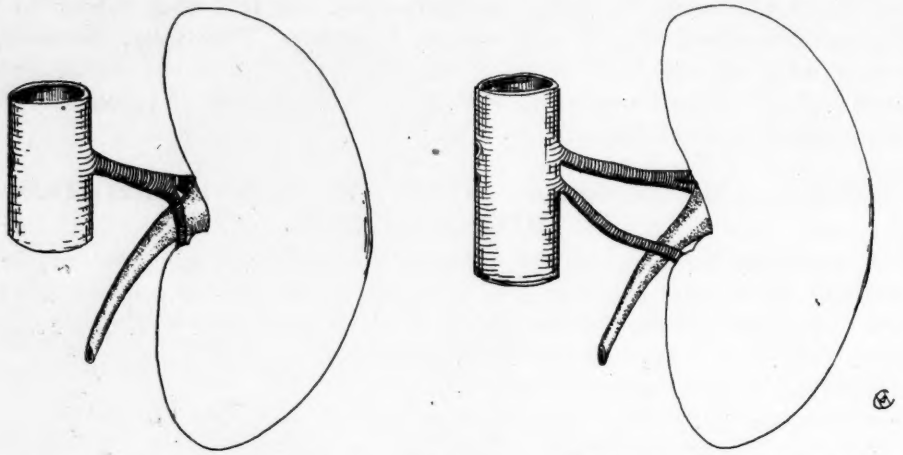


FIG. 179.—Posterior view of a left kidney, showing the same relationship between the normal inferior branch of the renal artery and the upper end of the ureter as in the preceding illustration. A, Anterior branches of artery; V, Vein; I, Inferior branch of artery; U, Ureter.

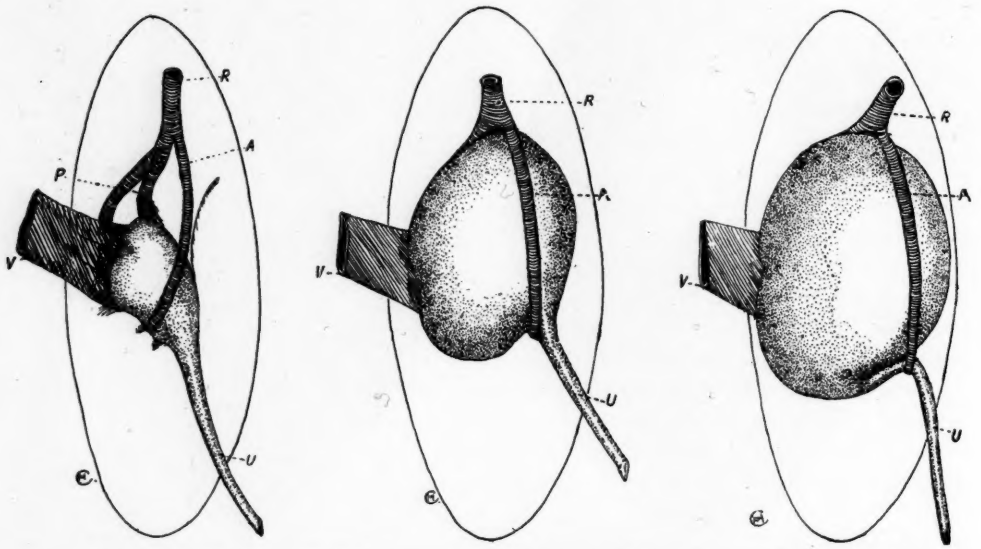
represent all the available local specimens in so far as my searches carry me through the various pathological museums of London. Before discussing

each of these individually, I will consider the normal arrangement of the blood-vessels in the hilum of the kidney.

I have dissected these vessels in 35 specimens and find that the common arrangement is for the renal artery to proceed towards the upper part of the hilum and there to divide into three main branches, two superior, which enter



FIGS. 180, 181.—Showing the extreme variations in origin of the inferior branch of the renal artery.



FIGS. 182, 183, 184.—Medial views of a series of renal hila. The renal vein has been turned forward to show the changing relationships between the pelvis, inferior artery, and ureter during the process of pelvic distension. R, Renal artery; A, Antero-inferior branch; P, Postero-superior branch; V, Vein; U, Ureter.

further into the hilum above the pelvis, and one inferior, which enters the lower part of the hilum by coursing downwards and outwards across the front of the pelvis. It will be seen that it is this normal inferior vessel, either venous or arterial, which commonly plays the important part of compressing

the ureter during the process of pelvic distention. From the relationship which both the inferior artery and vein have to the pelvis as seen in *Fig.* 177, a hydronephrosis would develop and progress without the ureter being implicated in any way by either of these vessels. In *Fig.* 178, which is a posterior view of a right kidney, the inferior artery enters the hilum by passing in front of the upper part of the ureter, thus allowing the pelvis to lie opposite the vascular space bounded above by the superior vessels and below by the inferior arterial branch. *Fig.* 179 is a posterior view of a left kidney where a similar relationship exists.

When the pelvis dilates it expands in all directions, but forwards more than backwards in conformity with the direction of least resistance. Should the pelvis in such circumstances lie opposite to the vascular interval just described, it will project into this gap, and in so doing the upper end of the ureter may be drawn with it and so compressed between the inferior artery and the distended pelvis, provided the vascular space is sufficiently large. The size of the space is obviously smallest when the inferior vessel arises from the parent trunk close to the kidney, and becomes progressively larger as this vessel takes its origin nearer to the origin of the parent stem. The interval is largest when the inferior artery arises actually from the aorta itself, as it not uncommonly does. These points are illustrated in the diagrams, *Figs.* 180 and 181.

Figs. 182, 183, 184 are a series of medial views of renal hila, and represent the changing relationship of pelvis, ureter, and inferior artery during the development of a hydronephrosis. The renal vein is turned forward, and in the first of the series a slightly dilated pelvis is seen, with the two superior arteries above, and the inferior branch passing in front of the pelvis. In the next one the distention has gone a little further, and the ureter has approached nearer to the inferior artery. In the last of the series the ureter is seriously compressed between the artery and the distended pelvis. The artery, which originally lay in front of the pelvis, is now behind that structure. Such a relationship explains the belief that the ureter becomes compressed by an aberrant vessel which passes behind the renal pelvis.

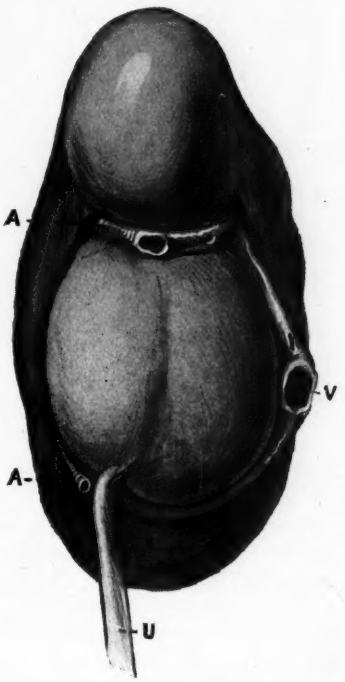


FIG. 185.—Medial view of a left hydronephrosis in which the commencement of the ureter has been kinked by the normal inferior branch of the renal artery. A, Artery; V, Vein; U, Ureter. (*From Guy's Hospital Museum, No.* 1693.)

The actual specimens which I have collected will now be considered. Five are from the Museum of Guy's Hospital, and one has been taken from the Museums of each of the following Hospitals: St. George's, St. Mary's, St. Thomas's, the Royal Free, and one from the Museum of the Royal College of Surgeons. I wish to take the opportunity

of thanking the curators of the Museums concerned for allowing me facilities to have these specimens illustrated.

Specimen 1.—*Fig.* 185 is a medial view of a left hydronephrosis. On the front of the distended pelvis, which is bulging slightly more forwards than backwards, lies the renal vein, of which the inferior tributary can be clearly seen. This vessel is normal in its point of exit from the renal hilum and its junction with the parent vessel. The two superior branches of the renal artery are seen entering the hilum above the pelvis, and their point of origin from the renal artery is evident.

A slight but definite kinking of the upper end of the ureter can be seen, and from the position of the remains of the inferior artery and from the presence of the vertical groove on the inner aspect of the pelvis, it is clear that this kinking was caused by contact with the normal inferior branch of the renal artery.

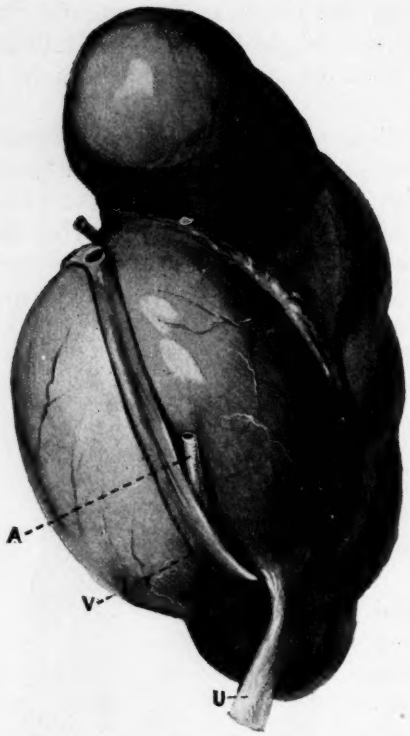


FIG. 186.—Postero-medial view of a right hydronephrosis, in which the normal inferior branch of the renal vein is compressing the commencement of the ureter. A, Artery; V, Vein; U, Ureter. (*From Guy's Hospital Museum*, 1920/63.)

Specimen 2.—*Fig.* 186 is a postero-medial view of a right hydronephrosis. One sees the forward bulging of the distended pelvis and the inferior vessels passing into the lower part of the hilum. There is obviously some commencing interference with the upper end of the ureter by the inferior vein, which is normal in its connection with the main venous renal trunk and in its point of exit from the kidney. The inferior artery, as in the last specimen, has been divided, but sufficient of it remains to indicate that it was a normal vessel. It is the vein in this case which appears to be in most intimate relationship with the ureter.

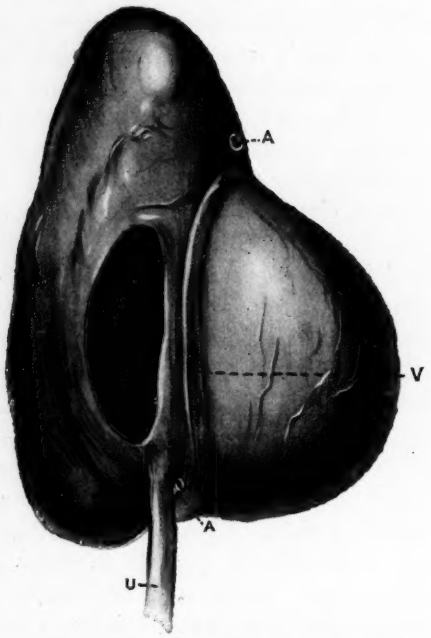


FIG. 187.—Posterior view of a left hydronephrosis. (*From Guy's Hospital Museum.*)

Specimen 3.—*Fig.* 187 is a postero-medial view of a left hydronephrosis. The inferior vessels are both seen. Neither is compressing the ureter, although each is in the vicinity. The inferior artery has been divided, but the course of its companion vein suggests the normal origin of the artery. It should be noted what a markedly posterior position on the pelvis the inferior vein occupies. In explanation of this,

I would call attention to the considerable forward projection of the pelvis, for the more this structure advances, the more posterior are the inferior vessels likely to become.

In this specimen these vessels are so markedly displaced that one wonders whether the present relationship was not already in existence before the dilatation occurred. If such were the case, it would be necessary that the vessel after passing downward behind the pelvis should curve forward round the inner border of the ureter, and enter the hilum after passing in front of this structure, as indicated in *Fig.* 188. Such a vascular anomaly, as far as I know, has never been described, and probably has never existed, but it is the only possible alternative to the explanation I have given.

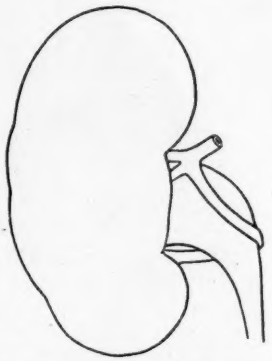


FIG. 188.—Posterior view of a left kidney, illustrating the kind of arterial anomaly that would be necessary were the relationship seen in the foregoing specimen pre-existent to the dilatation.

It will be noticed that in each of the foregoing examples the inferior artery has been divided by the surgeon close to its entry into the hilum. It would be obvious to the operator in each case that the vessel was lying somewhat posterior to the pelvis, but only by taking additional pains—often considerable on account of the pelvic distention, and unnecessary from the point of view of the nephrectomy—could the true origin of the vessel be established. Hence the false theory of hydronephrosis due to an abnormal vessel passing behind the pelvis and obstructing the ureter has arisen, and continues to receive support, for the condition I have described is a common one, and fresh examples are constantly being reported and misinterpreted.

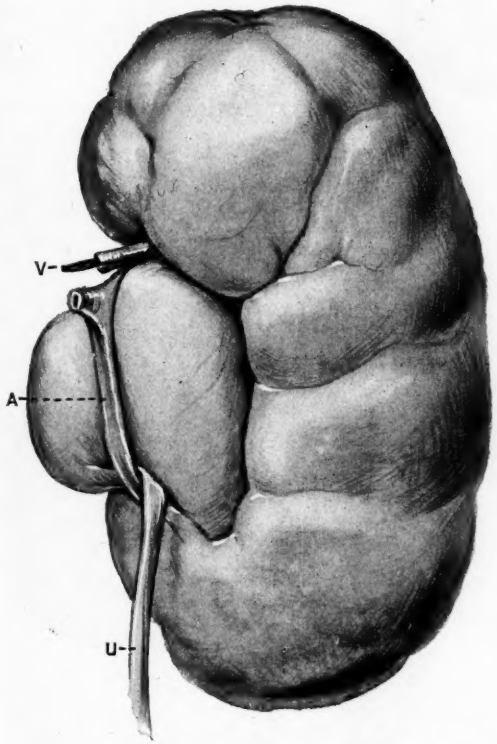


FIG. 189.—Posterior view of a right hydronephrosis, showing compression of the ureter by the normal inferior branch of the renal artery. V, Vein; A, Artery; U, Ureter. (*From Guy's Hospital Museum, No.* 1695.)

Specimen 4.—*Fig.* 189 is a posterior view of a right hydronephrosis. The artery which is the offending member is seen to be perfectly normal in origin and point of entry into the kidney. One can imagine in this example that by pulling the ureter downwards, so that the pelvis and upper part of the ureter were drawn backwards, the inferior artery and the pelvis would be restored to their normal relationship—namely, with the artery in front of the pelvis.

Specimen 5.—*Fig.* 190 is a posterior view of a left hydronephrosis. As in the previous example, the ureter is implicated by the normal inferior vessels, and here, as before, by pulling on the ureter the original relationship of the inferior vessels to the front of the pelvis could be restored.

Specimen 6.—*Fig.* 191 is a posterior view of a left hydronephrosis. The amount of pelvic distention here is very considerable, with a marked forward projection over the normal inferior artery, which is seen lying on the middle of the posterior aspect of the pelvis. The ureter has been dragged forward and has become markedly compressed.

Specimen 7.—*Fig.* 192 is a postero-medial view of a left hydronephrosis. Here also the pelvis has gone well forward, and the ureter has become involved, in this case by the normal inferior branch of the vein.

Specimen 8.—*Fig.* 193 is an antero-medial view of a left hydronephrosis. Here the inferior vein can be seen interfering with the upper end of the ureter. The corresponding artery has an independent origin from the aorta, and those who attach so much importance to such an origin must realize that the normal vein is playing a more important part than the abnormal artery.

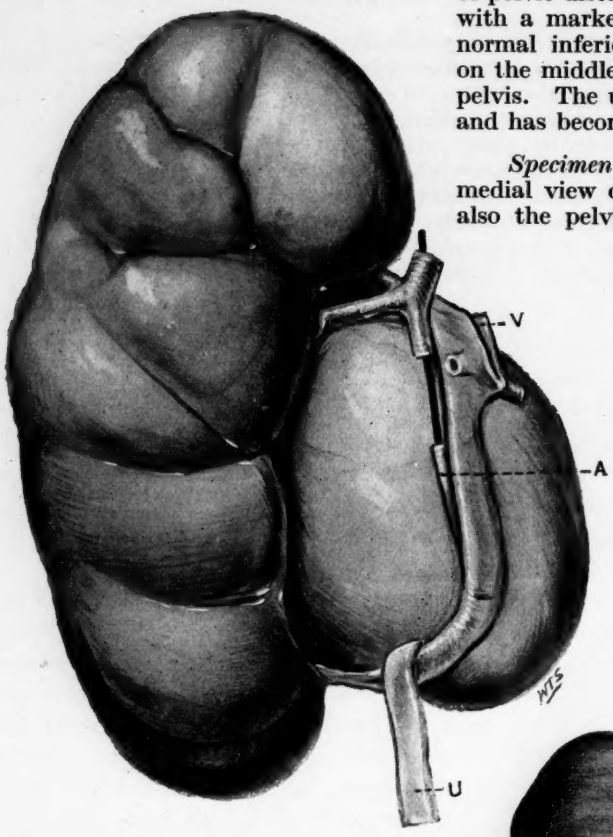


FIG. 190.—Posterior view fo a left hydronephrosis, showing a looping of the ureter over the normal inferior branch of the renal vein. V, Vein; A, Artery; U, Ureter. (*From Guy's Hospital Museum, No.* 1694.)

The interval between the upper and lower branches of the vein is not sufficient to allow the pelvis to bulge through to any great extent. Were the limiting influence of this venous circle not present, no doubt the aberrant artery would have produced a considerable looping of the ureter.

Specimen 9.—*Fig.* 194 is a posterior view of a right hydronephrosis. The inferior artery has its origin close to the aorta and has thus provided a very wide interval between the upper and lower arterial branches. As a consequence the pelvis has gone completely forward and a marked looping of the ureter has

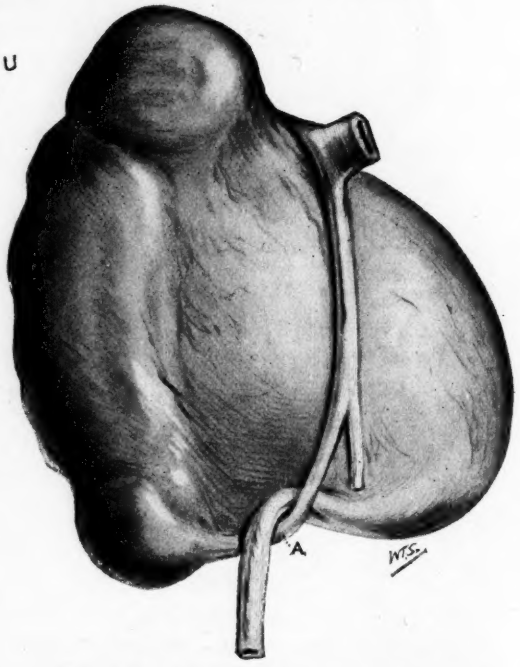


FIG. 191.—Posterior view of a left hydronephrosis. The pelvis has bulged forward over the normal inferior artery, which is compressing the ureter. (*From St. George's Hospital Museum.*)

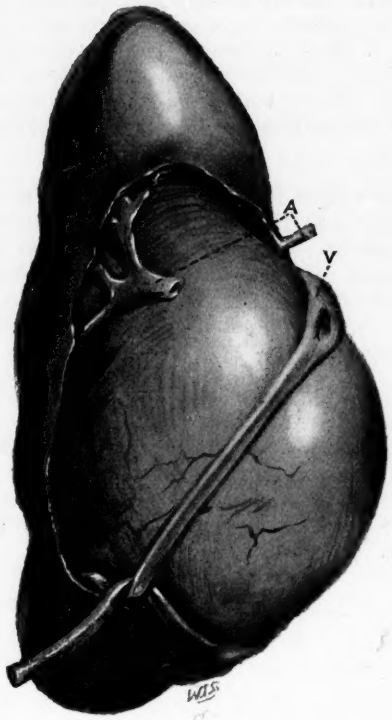


FIG. 192.—Postero-medial view of a left hydronephrosis. The pelvis has bulged forward through the interval between the superior and inferior branches of the renal vein. The inferior branch, which is quite normal, is compressing the ureter. A, Artery; V, Vein. (*From St. Mary's Hospital Museum.*)

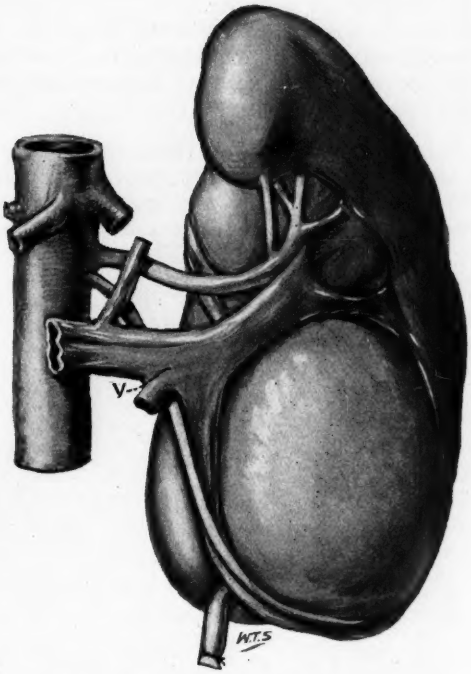


FIG. 193.—Antero-medial view of a left hydronephrosis. The ureter is compressed by the normal inferior branch of the renal vein. (*From St. Thomas's Hospital Museum.*)

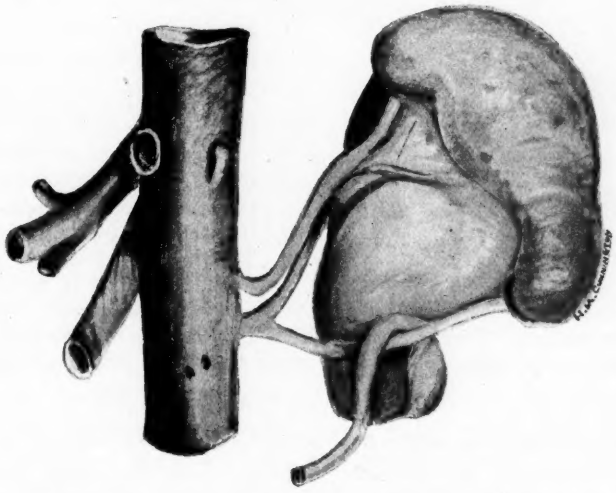


FIG. 194.—Posterior view of a right hydronephrosis. The ureter is looped over the normal inferior branch of the renal artery. (*From the Royal Free Hospital Museum.*)

taken place. That portion of the ureter which is proximal to the point of crossing of the artery is dilated, indicating the secondary obstruction which has arisen at this point. A slighter dilatation is noted for a short distance just beyond this, however, and no doubt it was here that the original obstruction arose. I have had an opportunity of examining this portion of the ureter under the microscope, and find it to be the seat of chronic inflammation which has resulted in narrowing of the lumen.

Specimen 10.—*Fig.* 195 is a posterior view of a right hydronephrosis. The pelvis has worked forwards between the superior artery and the inferior. The ureter is being compressed by the latter vessel, which has an independent origin from the aorta. This specimen represents the only genuine example amongst those I have put forward in which the ureter is being compressed by an abnormal artery.

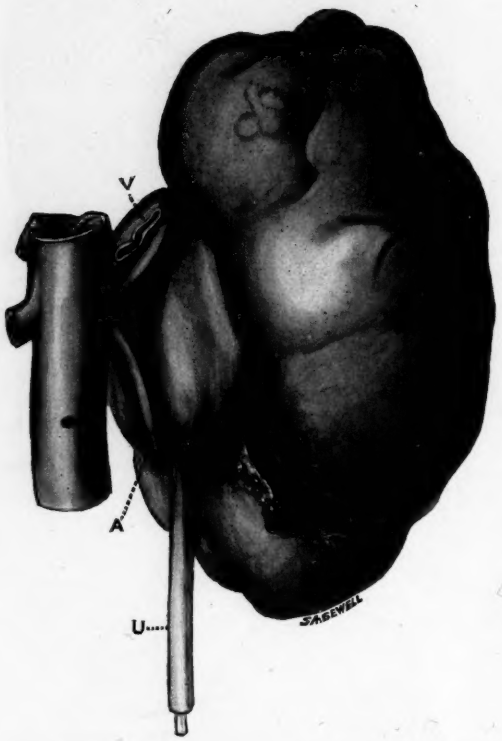


FIG. 195.—Posterior view of a right hydronephrosis. The ureter is compressed by the inferior branch of the renal artery, which is abnormal in the sense that it has an independent origin from the aorta. V, Vein; A, Artery; U, Ureter. (*From the R.C.S. Museum, No.* 3521b.)

Fig. 196 is an anterior view of a left hydronephrosis, illustrating an example in which the interval between the superior and inferior groups of renal vessels is not sufficiently large to allow the pelvis to come forward by this route.

I should like to call attention to yet another form of vascular involvement of the ureter. In certain cases there is a venous tributary to the left spermatic vein from the lower pole of the left kidney. The vein crosses superficially to the ureter, as seen in *Fig.* 177. Should the left kidney become the seat of a hydronephrosis in such a case, a marked kinking of the ureter over this venous tributary is likely to result.

Specimen 11 (*see Fig.* 166).—This is the posterior view of a left hydronephrosis where the complication mentioned above has actually taken place. The vein involving the ureter is seen to join the spermatic vein. The length of ureter proximal to the actual looping is much more than in any of the other examples. This is explained by the lack of obstruction to the forward progress of the pelvis resulting from the exceptionally wide vascular interval between the aberrant vein and the vessels above.

There is no doubt that some interference with the ureter by a renal vessel is exceedingly common in hydronephrosis. This is borne out by the fact that Mayo, in reporting on 27 cases, found some compression of the ureter by a blood-vessel in 20, and in all but 2 the offending arteries came from the renal trunk.

Among the numerous references in the literature to hydronephrosis there are very many in which an aberrant vessel is cited as the cause. In the large majority there is no detailed account of the actual origins of the vessels or of the points at which they leave the kidneys. In noting this lack of detail one bears in mind how difficult it is during an operation on a distended kidney to be sure of the origin of certain vessels. Papin and Iglesius call attention to this point. No doubt this difficulty has often led to the erroneous conclusion that a normal vessel is an abnormal one. Kuster, Israel, Bazy, Duval, Grégoire, and other able observers all reject the abnormal-vessel theory.

In a number of reported cases there is an illustration of the diseased kidney. In each one that I have seen there exists the same relationship between pelvis, ureter, and blood-vessels as was apparent in the series I have brought forward; moreover, although in many instances the vessel is described as abnormal, it is obviously a normal one.

Bazy gives a diagrammatic illustration of a different view of the development of the vascular complication. He shows the inferior vessel passing behind the ureter. He explains that the dilating pelvis sinks behind the artery, dragging the ureter with it. It must be a rare form of the disease, as none of my specimens shows it. It is difficult to understand in what circumstances the enlarging pelvis should not follow the line of least resistance, which is forwards and not backwards.

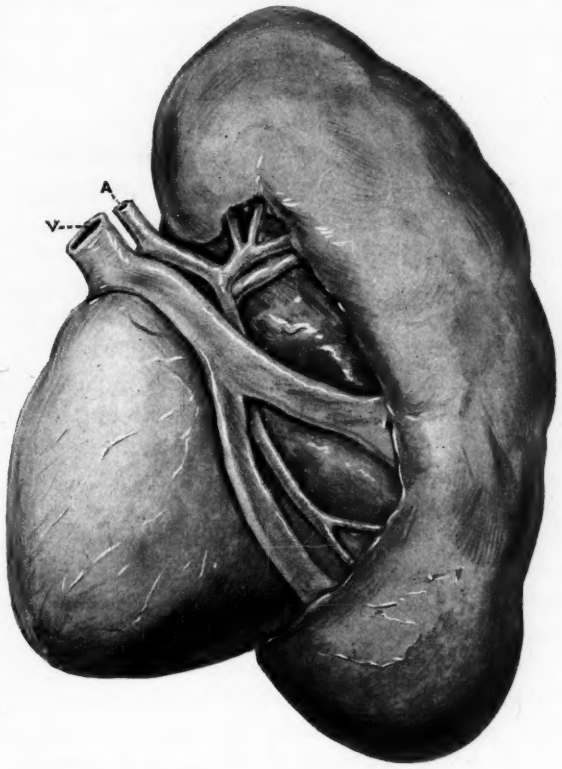


FIG. 196.—Anterior view of a left hydronephrosis, showing the relationship when the interval between the superior and the inferior branches of the renal vessels is not large enough for the pelvis to project through.

Marion supports the view that abnormal vessels are a cause of hydronephrosis, because in his cases he has found the vessel at the level of the constriction of the ureter. The answer to this is that the same relationship is found where the vessel concerned is a normal one. The same view has also a certain amount of support from the relief gained in certain cases after division of the constricting vessel. In this connection, however, it is instructive to turn to the report from the Mayo Clinic dealing with 503 cases of hydronephrosis operated upon between 1907 and 1923:—

In 17 cases cutting of anomalous blood-vessels was carried out, in 10 cases with a satisfactory result, and in 7 with an unsatisfactory result. In 9 cases nephropexy was carried out as well, with unsatisfactory results in 5 cases. The patients who were relieved by division of the blood-vessels were those whose symptoms were only moderate, or who had only a slight degree of dilatation.

In view of the definite narrowing which has occurred at the pelvic outlet in many of the more advanced cases, it is difficult to see how any cure could result in any but the earliest examples. On the other hand, in those cases in which there is a definite compression of the ureter on to the dilated pelvis there must obviously be some relief to the obstruction by dividing the vessel.

REFERENCES.—4, 6, 15, 16, 17, 20, 30, 31, 33, 38, 41, 50, 53, 58, 65, 72, 78, 79, 80, 82, 86, 87, 88, 97, 103, 105, 108, 121, 122, 128, 135.

SUMMARY.

1. Hydronephrosis with the dilatation beginning at the pelvo-ureteral junction is the commonest form of the disease. It occurs both as a congenital and an acquired condition.

2. Many cases of hydronephrosis have been reported in abnormally developed kidneys, but in what way these predispose to the disease is not known.

3. In a large proportion of the cases identified in fœtal and early child life, and which are undoubtedly congenital, the dilatation is bilateral and often involves one ureter or both ureters, while in some fœtal examples the lumen is completely obliterated.

4. In the great majority of cases of hydronephrosis the first manifestations of the disease are in adult life, most commonly between the ages of 20 and 30 years. In many of these the kidney is found to be in an extremely early stage of dilatation. It is therefore assumed that such cases represent the acquired form of the disease.

5. The earliest cases show narrowing of the ureter from chronic inflammation, and this appears to be the cause of the dilatation. In all cases there is an associated pyelitis, and some chronic interstitial nephritis.

6. Exacerbations of the existing pyelitis will explain the attacks of pain which come on without apparent cause in most cases of hydronephrosis. There is evidence of the infection either on cystoscopy or in the urine in a large proportion of cases during an attack of pain, which is often accompanied by increased frequency of micturition. There may be little or no evidence of infection after an attack has passed.

7. Chronic, or severe acute, inflammatory disease in any part of the body, chronic gastro-intestinal derangement, and the pyelitis of pregnancy are common antecedents of hydronephrosis.

8. There is no conclusive evidence that renal mobility is ever a cause of hydronephrosis.

9. Traumatism is a rare cause, and results from the contraction of scar tissue in the wall of an injured ureter.

10. In drawing conclusions from the specimens I have put forward illustrating a vascular complication of hydronephrosis, I would call attention to the following facts :—

a. They represent all the available examples demonstrating a vascular complication of a hydronephrosis, and throughout the whole series there is a complete uniformity in the mechanism producing this complication.

b. In 9 of the 11 examples the vessel implicating the ureter is a normal inferior branch of one of the main renal vessels. In some instances it is the venous and not the arterial branch. In none of these specimens is the artery implicating the ureter aberrant in the sense that it enters the kidney through the cortex and not by way of the hilum.

c. It is therefore concluded that the process here described is the usual one which determines a vascular complication of the ureter in certain cases of hydronephrosis. The aberrancy of the vessel concerned is not necessary, in fact occurs infrequently, but offers the most favourable opportunity for compression of the ureter to occur when present.

d. It is obvious, however, that ultimately the ureter may be seriously compressed between the vessel and the distended pelvis in certain cases, and therefore some relief is likely to result from division of the constricting vessel.

In conclusion, I wish to express my thanks to the Surgical Staff of the Royal Free Hospital, to each member of which I am indebted for material for this paper, and also to Dr. H. M. Cunnington for her assistance in the experimental work on rabbits, and in some of the histological work. Help from Mr. Ulysses Williams and Dr. Scott Williamson is also gratefully acknowledged. I have to divide my thanks between Dr. Cunnington, Mr. Thornton Shiells, and Mr. S. A. Sewell for the excellent illustrations that they have provided.

BIBLIOGRAPHY.

[1] AIMES and DELORD, *Jour. d'Urol. méd. et chir.*, 1919, viii, 285.
[2] ALBARRAN, *Ann. des Mal. des Org. gén.-urin.*, 1896, xiv, 987.
[3] ALEXANDER, *Med. Press and Circ.*, 1907, cxxxiv.
[4] ALEXANDER, *Ann. of Surg.*, 1910, li, 129.
[5] ALLISON, *Med. Record*, liv, 313.
[6] ALGLAVE, *Bull. et Mém. Soc. de Chir.*, 1923, xlix, 678.
[7] ALGLAVE and PAPIN, *Jour. d'Urol. méd. et chir.*, 1920, ix, 37.
[8] AUGIER, *Arch. gén. de Chir.*, 1911, vii, 646.
[9] BATTLE, *Med. Press and Circ.*, 1899, n.s., cxix, 117.
[10] BAGGIO, *Policlinico*, 1921, Nov. 15.
[11] BARD, *Jour. d'Urol.*, 1920, ix, No. 11, 243.
[12] BARD, *Ann. de Méd.*, 1916, iii, 567.
[13] BARNEY, *Ann. of Surg.*, 1917, lxv, 597.
[14] BAZY, *Bull. et Mém. Soc. Anat. de Paris*, 1893, lxviii, 224.
[15] BAZY, *Bull. et Mém. Soc. de Chir. de Paris*, 1904, n.s., xxx, 253.
[16] BAZY, *Ibid.*, 1923, 593.
[17] BAZY, *Ency. franç. d'Urol.*, 1914, Doin et Fils, Paris.
[18] BLACKWOOD, *Edin. Med. Jour.*, 1895–6, xli, 919.
[19] BLOCK, *Zeits. f. urol. Chir.*, 1923, xii, 219.
[20] BORELIUS, *Folia urol.*, 1912–13, vii, 621.
[21] BOURCY, *Semaine méd.*, 1898, xviii, 513.
[22] BRAASCH, *Jour. Amer. Med. Assoc.*, 1909, lii, 1383.
[23] BRAASCH, *Interstate Med. Jour.*, 1914, xxi, 1180.
[24] BRAASCH, *Jour. Amer. Med. Assoc.*, 1919, lxxiii, 731.
[25] BRYANT and HALE WHITE, *Guy's Hosp. Rep.*, 1901, lv, 17.
[26] BROCA and LESNÉ, *Bull. et Mém. Soc. de Pédiat. de Paris*, 1905, vii, 287.

[27] Cabot, *Boston Med. and Surg. Jour.*, 1907, xiv, 277.
[28] Carless, *Lancet*, 1909, ii, 1540.
[29] Carpenter, *Rep. Soc. Study Dis. Child.*, 1908, viii, 298.
[30] Chute, *Trans. Amer. Assoc. Genito-urin. Surg.*, 1922, xv, 65.
[31] Coats, *Glasgow Med. Jour.*, 1891, xxxv, 342.
[32] Cosens, *Lancet*, 1909, ii, 1469.
[33] Cottrell, *Urol. and Cutan. Rev.*, 1922, xxvi, 340.
[34] Cromwell, *Jour. Amer. Med. Assoc.*, 1922, 1103.
[35] Darget, *Jour. de Méd. de Bordeaux*, 1920, i, 247.
[36] d'Astros, *Bull. et Mém. Soc. de Pédiat. de Paris*, 1913, xv, 435.
[37] Davis, *Jour. of Urol.*, 1923, x, 40.
[38] Delbet, *Bull. et Mém. Soc. de Chir.*, 1905, n.s., xxxi, 1144.
[39] Delafosse, *Ann. des Mal. des Org. gén.-urin.*, 1892, x, 49.
[40] Delestre and Haret, *Bull. et Mém. Soc. Anat. de Paris*, 1900, lxxv, 1069.
[41] Duffield, *Long Island Med. Jour.*, 1916, x, 439.
[42] Dun, *Liverpool Med.-Chir. Jour.* 1904, xxiv, 197.
[43] Duplay, *Union méd.*, 1894, 3 s., lvii, 37.
[44] Duplay, *Ibid.*, 1896, ii, 265.
[45] Edwards, *Med. Press and Circ.*, n.s. lxxii, 335.
[46] Eisendrath, *Jour. Amer. Med. Assoc.*, 1911, lvii, 110.
[47] Erdman, *Ann. of Surg.*, 1909, xlix, 256.
[48] Footner, *Brit. Med. Jour.*, 1878, ii, 57.
[49] Ferron, *Bull. et Mém. Soc. de Chir.*, 1909, n.s. xxxv, 298.
[50] Gardner, *Ann. of Surg.*, 1908, xlviii, 575.
[51] Garvis de Ronville, *Bull. et Mém. Soc. Anat. de Paris*, 1894, lxix, 622.
[52] Gayet, *Lyon chir.*, 1923, xx, 525.
[53] Geraghty and Frontz, *Jour. of Urol.*, 1918, ii, 161.
[54] Gerrard-Marchant, *Gaz. des Hôp.*, lxvi, 593.
[55] Goodhart, *Trans. Clin. Soc. Lond.*, 1890–91, xxiv, 61.
[56] Griffiths, *Trans. Pathol. Soc. Lond.*, 1889–90, xi, 161.
[57] Grulee, *Pediatrics*, 1909, xxi, 146.
[58] *Guy's Hosp. Gaz.*, 1919, xxxiii, 130.
[59] *Ibid.*, 1922, xxxvi, 56.
[60] Harvie, *Ann. Gynecol. and Pediat.*, 1897–8, xi, 430.
[61] Hammersley, *N. Z. Med. Gaz.*, 1909, Aug.
[62] Hauch and Lohse, *Ann. des Mal. des Org. gén.-urin.*, 1910, i, 588.
[63] Herrick, *Cleveland Med. Jour.*, 1916, xv, 704.
[64] Hess, *Pediatrics*, 1909, xxi, 161.
[65] Hinman, *Sec. Cong. del Soc. Internaz. di Urol.*, 1924, i, 96.
[66] Hue, *Bull. et Mém. Soc. de Chir.*, 1893, n.s. xix, 627.
[67] Hunner, *Jour. Amer. Med. Assoc.*, 1908, l, 1328.
[68] Jessett, *Med. Press and Circ.*, 1900, n.s. lxx, 445.
[69] Kakels, *N. Y. Med. Jour.*, 1916, ciii, 547.
[70] Kelly and Lewis, *Surg. Gynecol. and Obst.*, 1914, xix, 601.
[71] Knox, *Lancet*, 1891, ii, 1384.
[72] Kummer, *Jour. d'Urol.*, 1922, xiii, 425.
[73] Landouzy, *Bull. et Mém. Soc. Anat. de Paris*, 1870, 326.
[74] Lane, *Lancet*, 1894, ii, 910.
[75] Larkin, *Liverpool Med.-Chir. Jour.*, 1893, xiii, 79.
[76] Launay, *Bull. et Mém. Soc. Anat. de Paris*, 1894, lxix, 892.
[77] Legueu, *Ann. des Mal. des Org. gén.-urin.*, 1896, xiv, 982.
[78] Legueu, *Ibid.*, 1904, xxii, 1361.
[79] Legueu, *Bull. et Mém. Soc. de Chir.*, 1904, n.s. 415.
[80] Lowe, *Proc. Med. Soc. Lond.*, 1885–6, ix, 246.
[81] Lucas, *Brit. Med. Jour.*, 1891, ii, 1343.
[82] Marion and Pakowski, *Bull. et Mém. Soc. Anat. de Paris*, 1912, lxxxvii, 412.
[83] Marion, *Bull. et Mém. Soc. de Chir.*, 1923, xlix, 574.
[84] Martin, *Rev. de Chir.*, 1895, xv, 324.
[85] Martin, *Bull. et Mém. Soc. de Chir.*, 1899, n.s. xxv, 708.
[86] Martin-du-Pan, *Rev. méd. de la Suisse Rom.*, 1917, xxxvii, 638.
[87] Mayo, *Jour. Amer. Med. Assoc.*, 1909, lii, 1383.
[88] Macarthy, *Ibid.*
[89] Mitsinkides, *Jour. d'Urol.*, 1922, xiii, 964.
[90] Moure and Thounenin, *Bull. et Mém. Soc. Anat. de Paris*, 1914–19, lxxxix, 2.
[91] Mynter, *Ann. of Surg.*, 1893, xviii, 658.
[92] O'Neil, *Trans. Amer. Assoc. Genito-urin. Surg.*, 1922, xv, 77.

[93] OEHLECKER, *Zeits. f. urol. Chir.*, 1922, July.
[94] PANNETT, *Brit. Jour. Surg.*, 1922, April, 509.
[95] PAPIN, *Ency. franç. d'Urol.*, 1914, iii, 960.
[96] PAPIN, *Ibid.*, 298.
[97] PAPIN and IGLESIAS, *Rev. de Gynécol. et de Chir. abdom.*, 1909, xiii, 625.
[98] PAPIN and AMBARD, *Jour. d'Urol.*, 1924, ii, 337.
[99] PAWLIK, *Rev. de Gynécol. et de Chir. abdom.*, 1897, i, 787.
[100] PÉHU, *Lyon méd.*, 1905, civ, 801.
[101] PIC, *Ibid.*, 1906, cvii, 472.
[102] PILLET, *Normandie Méd.*, 1919, xxxi, 36.
[103] PITT, *Trans. Pathol. Soc. Lond.*, 1891, ii, 1343.
[104] POIRIER, CUNEO, and DELAMARE, English trans. by Leaf, Archibald Constable & Co., 1903, 139.
[105] POUSSON, *Ann. des Mal. des Org. gén.-urin.*, 1910, i, 600.
[106] POYNTON, *Proc. Roy. Soc. Med.* (*Dis. Child. Sect.*), xvii, 3.
[107] QUINBY, *Trans. Amer. Assoc. Genito-urin. Surg.*, 1922, xv, 77.
[108] QUINBY, *Jour. of Urol.*, 1923, x, 45.
[109] RABOT and BERTIER, *Lyon méd.*, 1904, cii, 869.
[110] RAFIN, *Jour. d'Urol. méd. et chir.*, 1919, 121.
[111] RAFIN and BOECKEL, *Ency. franç. d'Urol.*, 1914.
[112] RECLUS, *Bull. et Mém. Soc. de Chir.*, 1894, n.s. xx, 782.
[113] ROBINSON, *Brit. Med. Jour.*, 1891, i, 405.
[114] ROUTIER, *Bull. et Mém. Soc. de Chir.*, 1893, xix, 360.
[115] ROUTIER and PICART, *Ibid.*, 1914, xl, 209.
[116] RUTHERFORD, *Glasgow Med. Jour.*, 1905, lxiii, 135.
[117] SAUNDBY, *Birmingham Med. Rev.*, 1889, xxvi, 155.
[118] SEELING, *Ann. of Surg.*, 1908.
[119] SETZKE, *Austral. Med. Gaz.*, 1899, xviii, 154.
[120] SCOTT, *Surg. Gynecol. and Obst.*, 1912, xv, 296.
[121] SCUDDER and DAVIS, *Boston Med. and Surg. Jour.*, 1908, clviii, 523.
[122] SCHOLL and JUDD, *Surg. Clinics N. America*, 1924, iv, 425.
[123] SIMPSON, *Glasgow Med. Jour.*, 1867–8, ii, 332.
[124] STEWARD, *Trans. Clin. Soc. Lond.*, 1905, xxxviii, 150.
[125] SYMONDS, *Trans. Hunter. Soc. Lond.*, 1890–91, 120.
[126] TRATTNER, *Jour. of Urol.*, 1924, ii, 1924.
[127] TUFFIER, *Bull. et Mém. Soc. Anat. de Paris*, 1893, lxviii, 435.
[128] TUFFIER, *Semaine méd.*, 1896, xvi, 153.
[129] WALTHER, *Jour. Amer. Med. Assoc.*, 1922, 733.
[130] WEEKS, *Boston Med. and Surg. Jour.*, 1887, cxvii, 507.
[131] WILLIAMS, *Trans. Pathol. Soc. Lond.*, 1887–8, xxxix, 152.
[132] WILLIAMS, *Proc. Roy. Soc. Med.* (*Dis. Child. Sect.*), 1915–16, ix, 1.
[133] WRIGHT, *Med. Chron.* Manchester, 1892–3, xvii, 145.
[134] LUDOWIGS, *Zeits. f. Urol.*, 1923, ix, 397.
[135] MARION, *Bull. et Mém. Soc. de Chir.*, 1923, xlix, 574.
[136] MICHON, *Assoc. franç. d'Urol.*, Proc.-verb. 1911, Paris, 1912, xv, 412.

TUMOURS OF THE TESTICLE: THE SPERMATOCYTOMA GROUP.

By F. GORDON BELL, Edinburgh and Dunedin.

In a previous paper published in The British Journal of Surgery for July, 1925, the teratoid group of testicular new growths has been described. Before passing on to consider the second relatively common type of neoplasm—the seminiferous or germinal-celled tumour, called variously spermatocytoma, seminoma, round-celled sarcoma, and embryonal carcinoma—it is necessary to give a brief account of the development and normal structure of the testis, as indicating lines of pathogenesis, more particularly of the seminiferous tumours.

The Secretory Apparatus of the Testis.—The early phases in the development of the human testis have still to be satisfactorily elucidated. We are concerned here more particularly with the origin of the seminiferous cells, about which two conceptions prevail:—

1. It is generally stated that the seminiferous cells are derived from the columnar germinal epithelium (mesothelium) which covers the genital ridge lying medial to the Wolffian body. This specialized epithelium is believed to grow down in the form of rod-like ingrowths into the subjacent mass of mesodermal tissue (mesenchyme) which outlines the future body of the testis. The surface connections are then lost and the germinal cells appear as solid anastomosing cords transversing the mesoderm. Some of the germinal epithelial cells are characterized by their large size and different staining reactions, and constitute the spermatogonia or primitive sex cells.

2. There are, on the other hand, the elaborate researches of Beard, who concluded from a study of the primitive sex cells in elasmobranchs that the germinal or sex cells are formed at a much earlier phase in the development of the embryo—the morula or blastula stage—and migrate through the entoderm into the genital area when the cœlom is formed. Certain evidence from very early human embryos would appear to support this interpretation. Beard's thesis, then, would derive the seminiferous cells, not from the mesothelium covering the genital ridge, but from primitive sex cells which are budded off the morula and, passing to the genital area, become associated with the mesothelial ingrowths and mesoblastic tissue which provide merely support and nourishment.

In either case the solid anastomosing genital cords enclosing the scanty spermatogonia ultimately acquire a lumen and constitute the early seminiferous tubules. Whether the seminiferous epithelium is derived from the mesothelium of the genital ridge or migrates there from the morula remains uncertain.

Structure of the Fully Developed Seminiferous Tubule.—The seminiferous cells are enclosed by a definite basement membrane surrounded by a thick hyaline layer, which again is encircled by a layer of connective-tissue cells.

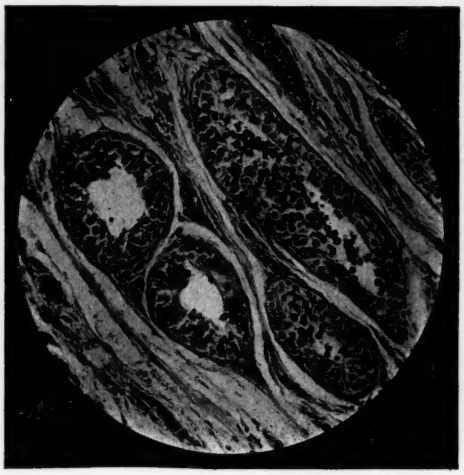


FIG. 197. — Normal testis, showing characters of the seminiferous or germinal cells.

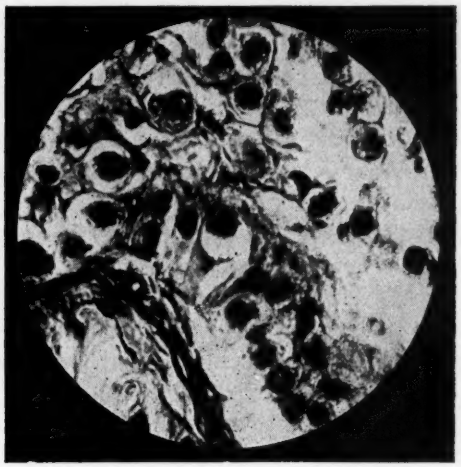


FIG. 198.—Normal seminiferous tubule: high power. The large round cells with clear-cut outline, granular nucleus, and clear protoplasm are spermatocytes.

The germinal cells are arranged in several layers possessing definite characteristics, which are briefly outlined, as having an important bearing on the interpretation of the germinal-celled tumours presently to be described.

1. THE SPERMATOGONIA.— These are rounded clear cells with a large round deeply-staining nucleus, and are set upon the basement membrane. Between them may appear elongated columnar cells which are not always easily made out. These are the sustentacular or nurse cells of Sertoli.

2. THE SPERMATOCYTES. — These are much larger oval or rounded cells disposed in one or more layers situated more centrally. Their nuclei often show various stages of active division.

3. THE SPERMATIDS OR IMMATURE SPERMATOZOA.—These appear as small protoplasmic cells with spherical nuclei lying still more centrally. The heads of the developing spermatozoa are said to retain some connection with the peripheral elongated nurse cells.

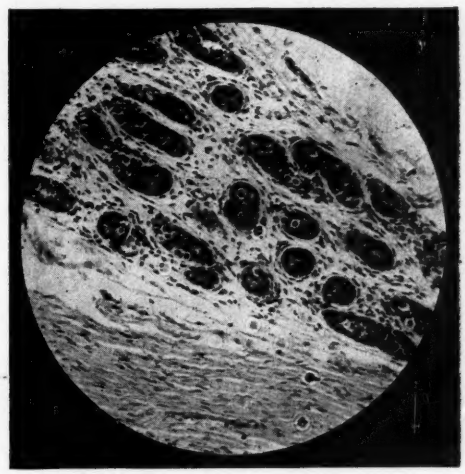


FIG. 199.—Testis from a boy, age 5, showing scanty spermatocytes, large cells with big nucleus and clear protoplasm.

The process of spermatogenesis, then, is as follows: The spermatogonia divide and produce the spermatocytes of the first order. These divide again,

producing the spermatocytes of the second order, which in turn divide and produce the spermatids or future spermatozoa. Cross-sections of the adult tubules show the appearances detailed above, though of course the phases of spermatogenesis vary in different tubules. The important point to note is that the cells are predominantly large and rounded, with a clear protoplasm and a large, deeply staining nucleus, and between the cells there is commonly observed a granular or even reticular framework (*Figs.* 197 and 198). Cross-sections of the immature tubule show chiefly an aggregation of small rounded, oval, or even tapering columnar cells with spherical nuclei (*Fig.* 199), the whole appearance closely resembling that of the early Graafian follicle with enclosed ovum.

The Excretory Apparatus of the Testis.—In some respects the testicle presents closer analogies with the kidney than with the ovary; for both in testicle and kidney we are dealing with secreting tubules developed in a special way which have to join up with an excretory apparatus, and in each case defects in fusion between the two sets of tubules have been alleged to account for tumour formations.

The excretory apparatus of the testicle is made up of the straight tubules, rete testis, vasa efferentia, epididymis, and vas deferens. These are all regarded as developed from the Wolffian system, though some doubt obtains about the origin of the straight and rete tubules. There are in addition certain vestigial remnants. The paradidymis, or organ of Giraldès, represents remains of isolated Wolffian tubules, while the hydatid of Morgagni is derived from the abdominal end of the Müllerian duct.

THE POSSIBLE PATHOGENESIS OF TESTICULAR TUMOURS.

The various tissues of the testis may now be considered from this aspect.

The Body of the Testis.—

1. The Seminiferous Cells (Epithelium).—We are uncertain as to the precise origin of these cells. Consensus of opinion, however, derives them from the germinal epithelium (mesothelium), and in this case we have the thesis of a specialized epithelium evolved from mesothelial tissues. If a malignant change supervenes, it appears possible that a *carcinoma* may develop from this specialized epithelium, a *sarcoma* from the undifferentiated mesothelium, and from a mixture of these two tissues or from the remarkably close interlocking of the mesothelium and subjacent mesoblast observed in the early stages of development, or from reversionary mesoblastic tendencies, *carcino-sarcomatous combinations* might arise. As a matter of fact carcino-sarcomatous features do occur in certain testicular tumours.

Regarding the seminiferous cells, tumour formations may be assumed to develop in two directions: (*a*) If the process of spermatogenesis runs wild, a carcinomatous tumour composed of cells of a special type may result. Such a tumour is well designated a *seminoma* or *spermatocytoma*, and is regarded by some as a common tumour of the testis. If, however, we regard the testis in the same light as any other secreting gland, we should expect simple adenoma of the seminiferous tubules to appear with fair frequency in relation to the malignant adenoma or seminoma, but adenoma testis of this variety

is rarely observed, though, like the small adenoma of the kidney, it may often escape detection. (*b*) If by any chance the sex cells are stimulated to segment—and in the early stages of development no essential difference can be made out between the sex cells of the ovary and testis—*teratomatous tumours* may result, for these cells, the öogonia and spermatogonia, are regarded as totipotent and capable of giving rise to any or all of the tissues of the body.

2. The Interstitial Cells.—These special and distinctive cells, serving the purpose of providing the internal secretion of the testis, are usually derived from the germinal epithelium, though regarded by some as of simpler connective-tissue origin. The interstitial tissue is often increased in the imperfectly descended testis, and its production can be stimulated by ligature of the vas deferens. In rare cases it may be so abundant as to constitute a definite tumour formation.

3. The Fibrovascular Stroma.—This is derived from the mesoblast of the genital ridge, and may be expected to give rise occasionally to tumours composed of purely mesoblastic tissue, e.g., fibroma, chondroma, osteoma, lipoma, myoma, endothelioma, sarcoma, and various combinations of these. Metaplasia might be assumed to produce the chondroma and myoma, which are of more particular interest; but as a matter of fact pure connective-tissue tumours are decidedly rare in the testis, though such tissues are common in the teratomata.

The Straight Tubule.—Rare tumours called Wolffian carcinomata, to distinguish them from the seminiferous cancers, are related by some to the cubical lining epithelium of the straight tubule, and are considered by others to be of dubious existence.

The Rete Testis.—The complicated network of canals called the rete is lined by a flattened or cubical epithelium, supported by a considerable amount of fibrous tissue. The rete is the meeting place where fusion of the secreting and excreting tubules normally occurs, but it is reasonable to suppose that some of the secreting tubules may occasionally fail to join up with the excretory apparatus and that this may initiate in the blind tubules an uncontrolled process allied to spermatogenesis. Mixed elements or 'rests' are not infrequent in this area in early life; lastly, it is a significant fact that new growths often begin in or near the rete, as Curling[1] showed by a process of exclusion.

Epididymis and Vasa Efferentia.—Primary malignant disease of the epididymis is of extreme rarity, which appears to point to a relative immunity of the Wolffian derivatives.

To summarize from my observations on a comparatively large number of testicular tumours, there appear to be two clear-cut types, both developing from the reproductive cells themsleves.

The first group—the *teratoid*—has been considered with many of its variations in a previous paper. It most probably arises from the segmentation of an aberrant germinal cell, incited by some stimulus at present imperfectly understood.

The second group—the *germinal-celled* tumour—arises from an uncontrolled

proliferation of the seminiferous cells forming the glandular system of the testis in precisely the same way as carcinoma of other glandular organs.

Chevassu,[2] who formulated his classification of testicular tumours on the structural basis detailed above, found that the germinal-celled type, for which he coined the name of *séminome*, and the teratoid variety appeared in almost equal proportions (59–61) in his series of 128 tumours. In my series the proportion has been approximately two to one in favour of the teratoid group, though it is probable that Chevassu's larger series yields a truer estimate of the relative frequency of the two types.

Other varieties of neoplasm can, I think, certainly be regarded as extremely rare, though simple or malignant tumours of connective-tissue origin may be expected to crop up from time to time in any large series. One of my specimens appeared to be a mixed-celled sarcoma developing from the stroma of the testis. No definite example has appeared of lympho-sarcoma testis, which presents several interesting and peculiar features, but I am inclined to think that some of the germinal-celled tumours may readily be mistaken for it.

The germinal-celled group now falls to be considered. Only a few specimens are described, and these are lavishly illustrated by microphotographs with the object of providing a conclusive demonstration of the origin of the germinal or seminal-celled tumour from the seminiferous epithelium.

THE SPERMATOCYTOMA GROUP.

At first sight it would appear entirely reasonable that the normal process of spermatogenesis should occasionally run riot, so to speak, and give rise to tumours composed of germinal cells and aptly designated spermatocytoma or seminoma, for we have to do with an organ in which cell multiplication proceeds on an enormous scale throughout the greater part of life, and it would seem highly probable that some factor—be it trauma or what not—may occasionally incite a blastomatous process and divert the normal spermatogenesis into a malignant channel. The problem, however, is not so simple as it may appear, and the capacity of the highly specialized cells lining the seminiferous tubules to give rise to a characteristic type of carcinoma called spermatocytoma or seminoma has been alike affirmed and denied by various observers.

Birch-Hirschfeld as far back at 1878 claimed to have traced all stages in the transition from the normal seminal tubules to the malignant phase. The extensive researches of Chevassu, published in 1906, focused attention on this tumour. Chevassu's work appears to have influenced French opinion, and Debernardi[3] and others followed his lead, the controversy then turning in the direction of settling the origin of the tumour from the cells of fully developed seminal tubules, or from unutilized 'rests' which have failed to unite with the seminal system (Pillict's thesis). Nicholson[4] (1907) accepts a spermatogenic origin for the carcinoma group of his large series, and recent papers indicate that the spermatocytoma has received wide recognition. Tanner[5] records 62 per cent of his collected series of 101 testicular tumours as spermatocytoma, while Southam and Linnell[6] are recent whole-hearted advocates.

Ewing,[7] on the other hand, describes this group as embryonal carcinoma arising from a one-sided development of a teratoid tumour, and raises the following objections to the spermatogenic origin advocated by Chevassu and others :—

1. The characteristic structure is often seen in teratomata—adult or embryonal.

2. In a very early embryonal carcinoma, minute traces of cartilage, entodermal alveoli, and squamous epithelial cell groups were present.

3. The rapid growth of the malignant element gives unusually favourable opportunity for the overgrowth and suppression of other elements.

4. The only known tumour of the adult spermatoblasts (the adenoma testis of Chevassu and others) is very different from the embryonal carcinoma.

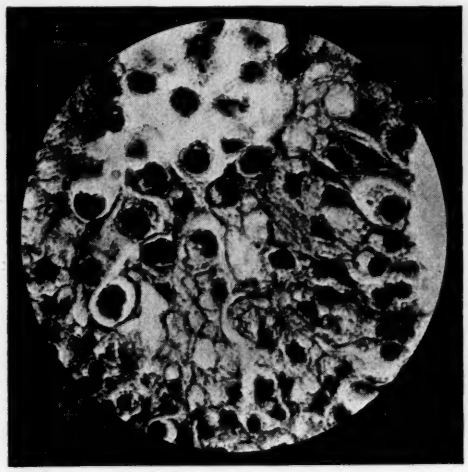


FIG. 200.—Seminoma or spermatocytoma, same power as *Fig.* 198, showing the remarkable similarity between the tumour cells and the spermatocytes in that figure.

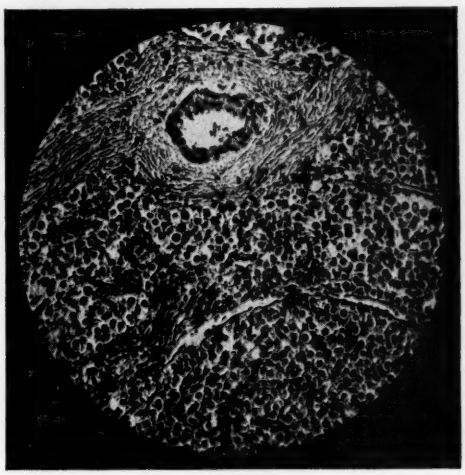


FIG. 201.—Seminoma or spermatocytoma, same power as *Fig.* 199, showing the striking resemblance between the type of cell in this tumour and the spermatocytes in that figure.

In a previous communication on teratoma testis reference has been made to an undifferentiated round-celled embryonal carcinoma arising from the glandular epithelial elements in certain teratomata and appearing in patchy distribution. Should a one-sided overgrowth take place along these lines and by suppression of the other elements transform the tumour into a pure or almost pure carcinoma, the histological appearances might closely resemble those of the germinal tumour presently described. One would expect, however, such an embryonal cancer to progress rapidly in common with other teratoid cancers, and, as will be shown presently, the germinal tumours are often characterized by a comparatively slow growth.

Several factors have convinced the writer that a specific tumour which may be called seminoma or spermatocytoma, to indicate its origin from spermatogenic or germinal cells, exists beyond all shadow of doubt, though the investigation of this collection of testicular new growths was begun with

rather a bias towards the teratoid theory. These factors may be briefly enumerated :—

1. It is possible to trace transitions between the normal or almost normal seminiferous tubules and the frankly malignant tissue. The evidence backing this statement is submitted in a series of microphotographs (*Figs.* 204 to 221), and if accepted nothing further need be said.

2. The cells of certain tumours are so specific in type that they must have a common origin, and by a process of elimination this origin is best fulfilled by the characteristic cells of the seminiferous tubules (*Figs.* 197 to 201).

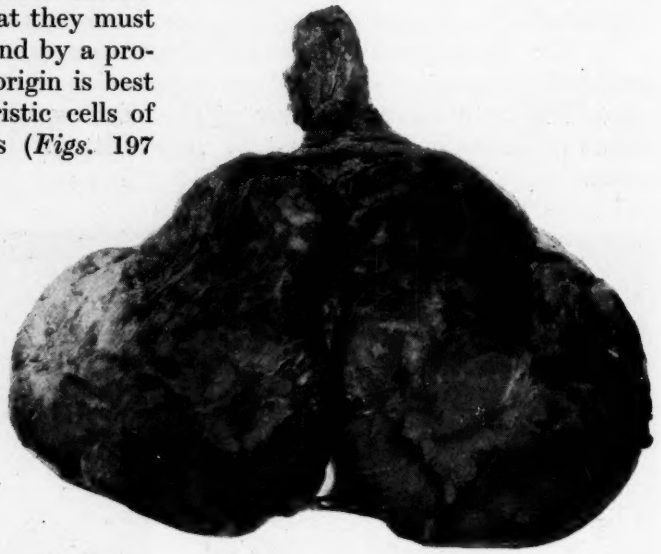


FIG. 202.—Seminoma of three years' duration. The cut surface displays the solid fleshy look so often seen in these tumours. The pale areas microscopically are undergoing degeneration, but have the same structure as the rest of the tumour.

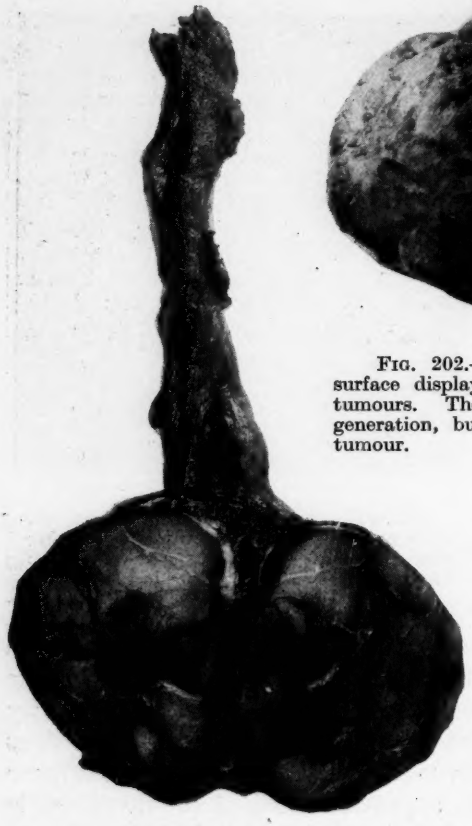


FIG. 203.—Seminoma of two years' duration. The cut surface is lobulated, solid, and fleshy, and lobulation is evident at the periphery. The epididymis, even after two years, is not incorporated.

3. The macroscopic appearances of many, but not all tumours of this variety, suggest that they belong to a specific type (*Figs.* 202, 203).

4. In two teratomatous tumours the cells of the peripheral isolated seminiferous tubules showed signs of proliferation and infiltration, and suggested the possibilities in this direction.

5. The combination of carcinomatous and sarcomatous features in some testicular tumours is more than coincidence, and the explanation must be sought in the early developmental phases of the secreting elements of the testis when mesothelial tissue begins to evolve in an epithelial direction, the carcino-sarcoma being a mixture of these acquired epithelial and reversionary mesoblastic characters. This matter will be discussed later.

6. The frequent origin of this group of tumours in middle life (*see* quoted histories) is suggestive; but this point should not be unduly stressed, for carcinoma of teratoid origin is not uncommon in the forties.

DESCRIPTION OF SPECIMENS.

Specimen 1 has been studied by the 'whole section' method and will be described in detail, the others more briefly. Fortunately the clinical histories are available, and the specimens are all in a good state of preservation.

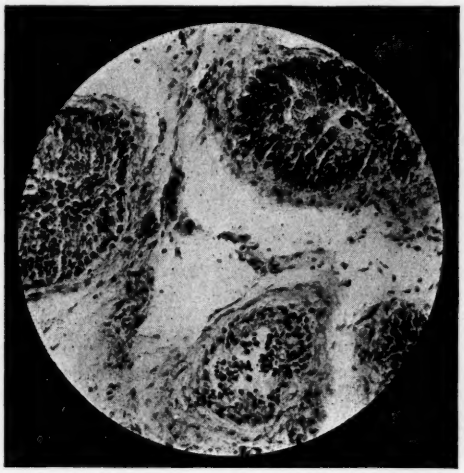


FIG. 204.*—*Specimen* 1. Seminiferous tubules persisting near upper pole.

* In *Specimens* 1 to 5 the first microphotograph is taken from the remains of the testis and the others from different areas of the tumour.

FIG. 205.—Same tumour. Note reduction in stroma, alveolar formation, and general resemblance of cells to *Fig.* 204.

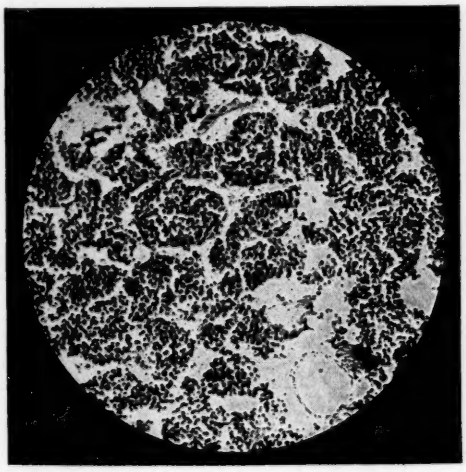


FIG. 206.—Same tumour. Lower power. Note alveolar formation and proliferation of the germinal cells, with reduction of stroma.

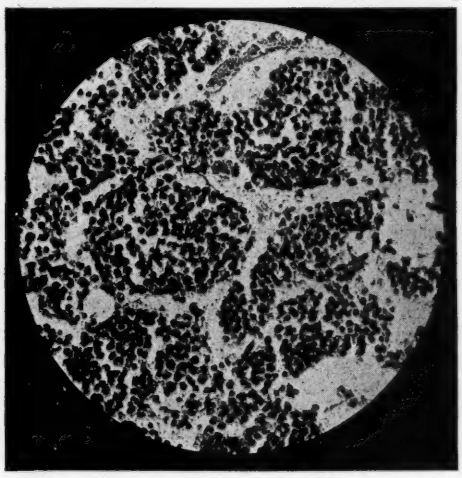


FIG. 207.—Same tumour, showing alveolar formation and character of cells.

Specimen 1.—(Labelled round-celled sarcoma.) The tumour was removed from a man, age 47, who had noticed a swelling of the testicle for nearly two years.

MACROSCOPIC.—The tumour is the size of the closed fist. The cut surface is firm, fleshy, and homogeneous, and is divided into lobules by septa. The epididymis is not invaded.

THE MICROSCOPIC FEATURES (*Figs.* 204, 205, 206, 207).—These may be described under the following heads :—

1. *The Character of the Cells.*—The alveoli are lined by round clear-cut cells with a large round deeply stained nucleus surrounded by a considerable amount of clearer protoplasm. These cells may appear in several layers and form the greater part of the cellular content of the alveolar groups, resembling to a marked degree the peripheral layer of germinal cells of the normal seminiferous tubules. There is, in addition, another type of cell, less numerous but more striking owing to its size. These are much larger rounded or ovoid cells, which lie more centrally and appear to have some connection at their bases with the smaller peripheral round cells. Their nuclei are of great size, often show a nuclear reticulum, and active division is going on apace—in short, they recall at once the large spermatocytes of the normal seminiferous tubules, and together with the other cells the whole appearance suggests irresistibly an uncontrolled process closely allied to spermatogenesis. In certain areas the smaller cells predominate and assume an oval or spindle shape. Many of the cells are strongly eosinophil.

2. *The Arrangement of the Cells.*—A definite alveolar arrangement is readily made out and persists in most parts of the section, though in places irregular cellular patches occur as the result of destruction of the alveolar walls.

3. *The Type of Blood-vessels.*—The blood-vessels in the main are well formed and are typical enough of spermatocytoma as usually depicted, or of carcinoma ; but here and there they are of the more embryonic type associated with sarcoma, though confined to the scanty stroma and not appearing between the individual cells.

4. *The Remains of the Testis.*—Testicular substance can be identified as scanty seminiferous tubules located near the upper pole in a portion of the section separated from the rest by an indefinite capsule. Some of these tubules show active proliferation (spermatogenesis) of a fairly normal type, recalling strongly the features of the neoplastic tissue described above, but, what is more significant, a few tubules contain clumps of cells indistinguishable from those of the malignant tissue. If the appearances just detailed are correctly interpreted, then the tumour is certainly a spermatocytoma, and these isolated tubules form the link between the normal and the malignant. A few degenerated tubules also persist at the lower pole.

5. *Other Elements.*—None appear in the various sections indicative of a tridermal origin.

Now let us consider alternative diagnoses :—

1. *The Cellular and Vascular Characters.*—The cells as described may be interpreted as evidence of a sarcomatous process. Indeed, there is little doubt that at first sight the tumour would be regarded by many as a large round-celled sarcoma exhibiting an alveolar arrangement. The blood-vessels are in the main too well formed for sarcoma, and alternatively it stands interpretation as an embryonal carcinoma, thus providing an illustration of the difficulty of differentiating between sarcoma and carcinoma testis.

2. *The Remains of the Testis.*—The fact that testicular substance is present at the upper pole of the testis and is separated from the main mass by an indefinite capsule may be variously regarded. It may represent the remains of the testis which has been isolated by the overgrowth of an encapsuled tumour, as is so common with teratomata. The tumour, then, is most likely to be an embryonal carcinoma of teratoid origin, but at the same time it is possible in a compartmented organ like the testis, which is divided into a number of lobules by fibrous septa, for a carcinoma, sarcoma, or spermatocytoma to involve only a part of the gland, and as the tumour progresses it may crowd one sector to the periphery and lead to an appearance of encapsulation by a condensation of fibrous tissue which really represents a fibrous partition.

Comment.—The balance of evidence is in favour of spermatocytoma arising from an exaggerated process allied to spermatogenesis, and the testicular substance near the upper pole provides the link in the conversion of the seminiferous tubules into the malignant germinal tissue.

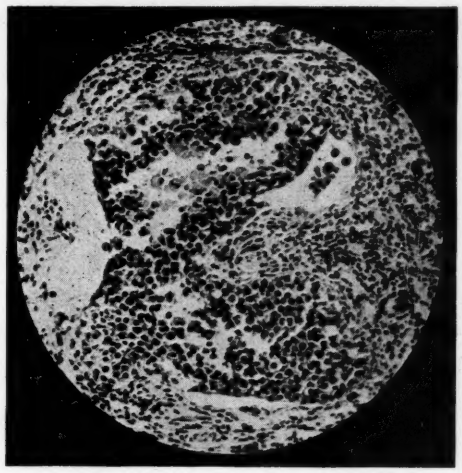


FIG. 208.—*Specimen* 2. Seminiferous tubule from remains of testis at lower pole showing proliferation of the germinal cells and invasion of stroma.

Specimen 2.—(Labelled round-celled sarcoma.) The tumour was removed from a man, age 52, who for three years had noticed that the right testicle was swollen and hard, though not painful till the last two months.

MACROSCOPIC.—The specimen is bisected, is roughly pear-shaped, and the size of the closed fist. The cut surface is firm and fleshy, with scattered paler patches and occasional small hæmorrhages. The epididymis is incorporated and indistinguishable. A small piece of granular testicular substance persists at the lower pole.

MICROSCOPIC (*Figs.* 208, 209, 210).—The structure in the main is that of an alveolar carcinoma, though there are abundant encephaloid areas. The cells are of the germinal type, rounded with clear cytoplasm and a large round deeply-staining nucleus. In some areas the alveoli are small and resemble cross-sections of the seminiferous tubules, and in other parts take the form of long parallel columns, not unlike adrenal cortex, these appearances depending on whether the tubules have been cut transversely or longitudinally.

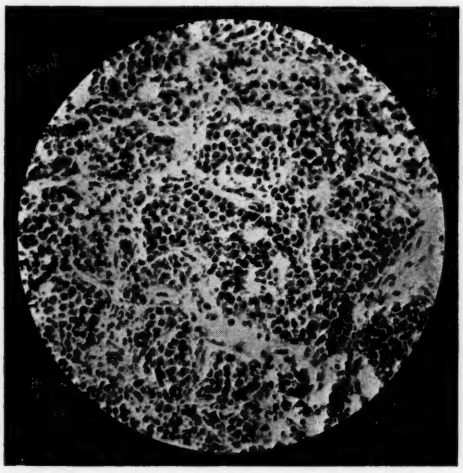


FIG. 209.—Same tumour. Alveolar formation still present though the walls of the tubules have mostly disappeared. Tubules cut transversely.

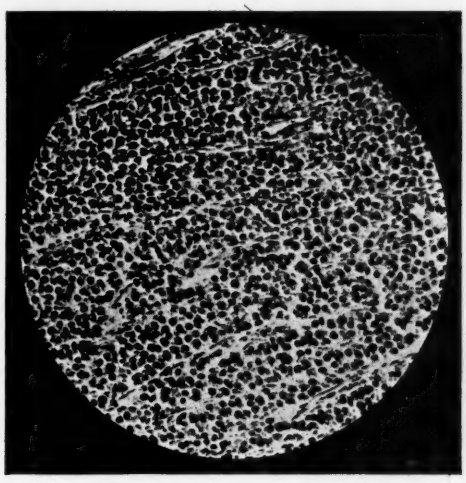


FIG. 210.—Same tumour. Tubules cut mostly longitudinally, the germinal cells appearing as broad sheets with scanty stroma. The tumour cells in *Figs.* 209 and 210 appear identical with those in *Fig.* 208.

The Blood-vessels are mostly well formed, though in some areas thin walled and sarcomatous in type.

Testis.—A small piece of testicular substance appears at the lower pole and the tubules are nearly all degenerated, but one shows both proliferation and infiltration.

Comment.—(1) The specimen is a typical example of the specific germinal-celled tumour, and the type and arrangement of the cells leave no doubt as to their origin. Epithelial characters predominate, but are mixed with sarcomatous features which justify to some extent the attached diagnosis. (2) The epididymis is incorporated. It is stated that the epididymis long remains free in this type of tumour, and this is certainly so in smaller examples, but this particular tumour was of long duration and comparatively large, and the germinal cells have therefore had every chance to infiltrate the epididymis. (Contrast with following specimens.)

Specimen 3.—(Labelled round-celled sarcoma.) This tumour was removed from a man, age 39, who gave a history of two years' painless swelling of the right testis.

MACROSCOPIC.—The specimen is bisected, is the size and shape of a large orange, and has a lobulated surface. The cut surface is divided into two areas. Near the mediastinum there is a small, roughly circular area showing hæmorrhagic infiltration, while the peripheral part is solid, fleshy, and homogeneous and not unlike normal testicular tissue, though less granular.

The epididymis is not involved.

MICROSCOPIC (*Figs.* 211, 212, 213, 214).—

FIG. 211.—*Specimen* 3. Section taken from peripheral part of tumour, showing near centre a recognizable seminiferous tubule cut longitudinally. The resemblance between the seminiferous cells and those of the surrounding malignant tissue is to be noted.

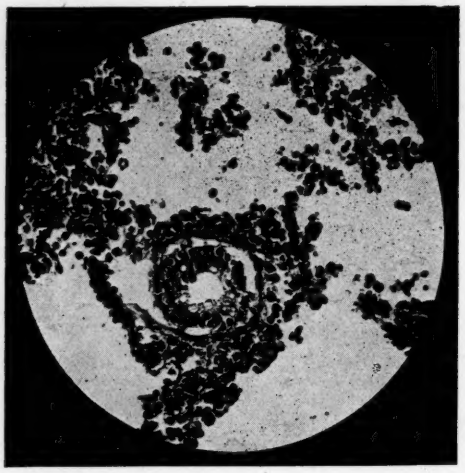


FIG. 212.—Same tumour, showing similar appearances. Seminiferous tubule cut transversely surrounded by frankly malignant tissue.

1. *The peripheral fleshy area* displays the features of the specific germinal tumour and—what is more important—scanty seminiferous tubules persist, and the transitions from these into the tumour tissue can be traced. The blood-vessels are in the main well formed. Scattered nodules of lymphoid tissue are present.

2. *The central hæmorrhagic area* displays another structure, also of a highly specific nature. It is definitely adenocarcinomatous, here and there papillary in

type, and has fairly abundant stroma. Many of the cells are remarkable for their large size, and are rounded, pyriform, or polyhedral with large darkly-staining nucleus. The adenocarcinomatous tissue shades off into the surrounding round-celled tissue without any line of demarcation. In the papillary areas, cross-sections yield a spurious peritheliomatous appearance, the large cells being disposed around a highly vascular core.

Comment.—(1) The cortical germinal-celled area calls for no remark except to say that its derivation from the seminiferous tubules seems beyond question. (2) The adenocarcinomatous area requires further consideration. The writer regards it as a highly specialized carcinomatous development of the mesothelial cells of the seminiferous tubules, and if reference is made to

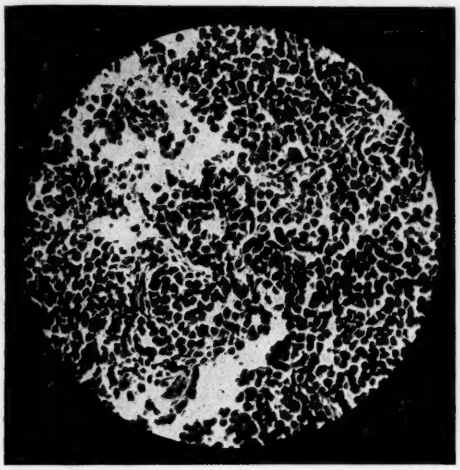


FIG. 213.—Same tumour as *Fig.* 211, showing general structure. Alveolar arrangement recognizable in parts.

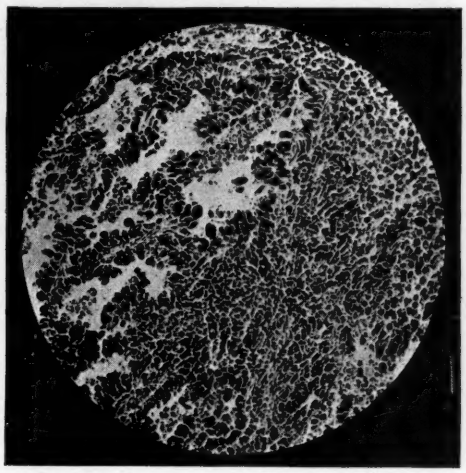


FIG. 214.—Same tumour. Section from junction of typical round-celled structure and adeno-papillary formation. The size of many of the cells in the latter should be noted.

the ovary a precisely similar appearance has been described under the heading folliculoma malignum. The papillary adenocarcinomatous tissue comes rather as a surprise in association with the typically germinal neoplasm, but I think it may reasonably be assumed to arise from germinal epithelium because :—

a. Similar appearances are sometimes seen in ovarian tumours, presumably arising from the mesothelial cells of the Graafian follicle.

b. Intermediate stages can be traced in other tumours between the typical seminoma and the large-celled carcinoma described above, and consequently a common origin from the germinal cells seems likely.

Specimen 4.—(Labelled carcinoma.) This tumour was removed from a man, age 47, who had noticed a swelling of the testicle for ten months.

MACROSCOPIC (*Figs.* 215, 216, 217).—The structure essentially is that of the specific germinal tumour and is predominantly carcinomatous, with variations in different areas. The cells are arranged in small alveoli or in large sheets, and are

mostly round or pyriform, but here and there are definitely spindle. In some areas the structure resembles adenocarcinoma and provides an intermediate phase between the typical seminoma and the papillary adenocarcinoma described in the previous specimen.

The early stages in the formation of a lymphoid stroma are well exhibited, the lymphocytes appearing along the line of the vessels in the supporting stroma. The testicular substance present at the lower pole is partly atrophied, but some of the seminiferous tubules show highly active proliferation.

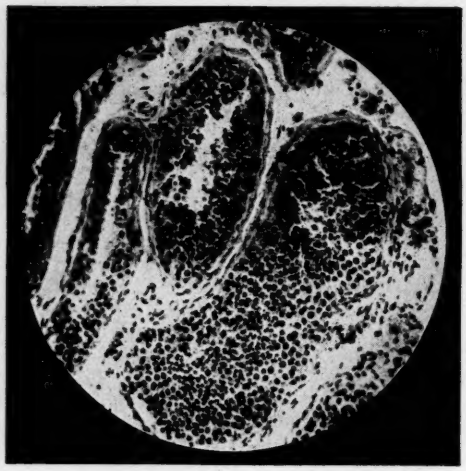


FIG. 215.—*Specimen* 4. Section taken from remains of testis persisting at lower pole, showing seminiferous tubules. The germinal cells are proliferating, and in the largest tubule are beginning to burst through the thinned capsule.

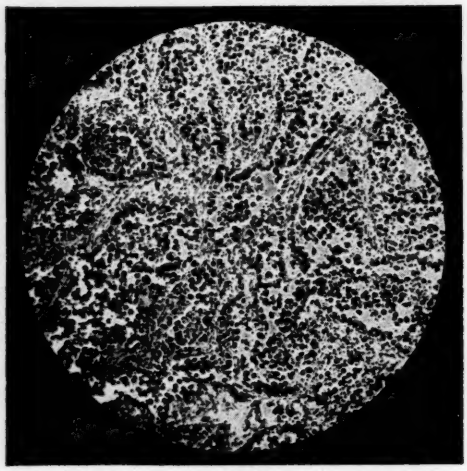


FIG. 216.—Same tumour. The germinal cells retain a well-marked alveolar formation. Along the line of the vessels in the stroma lymphocytes are beginning to appear—the forerunner of the lymphoid stroma seen in some other seminomata.

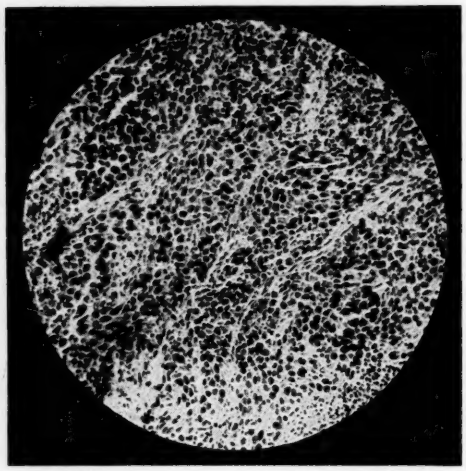


FIG. 217.—Same tumour, showing mixture of round and spindle cells.

Comment.—The tumour is a seminoma, but presents variations from the typical round-celled structure. It is noteworthy that this is the only tumour in the series labelled carcinoma, but parts might well stand interpretation as sarcomatous.

Sub-group : **CARCINO-SARCOMA.**

I propose now to describe a sub-group of germinal tumours under the heading of carcino-sarcoma. These are essentially germinal-celled tumours ; but as there is a tendency in some quarters to ignore the sarcomatous potentialities of certain testicular tumours, it seems necessary to state emphatically that combined carcino-sarcomatous features have been observed in a definite percentage of the present series. This peculiar feature as observed in the germinal-celled tumours should not be confounded with carcino-sarcomatous features sometimes seen in the teratoid tumour group, where epithelial and mesoblastic elements may proliferate concurrently and each element contributes to the mixture of malignancy. In the germinal-celled tumour the carcino-sarcomatous potentialities are inherent in the germinal cells themselves, and the connective-tissue stroma takes no part in the formation of the combined tumour.

It is a striking fact in the literature of 'medullary' testicular tumours that doubt often arises as to whether a particular tumour is a carcinoma or sarcoma. So acute an observer as Billroth said that he was often in doubt as to the precise nature of the medullary tumours. This difficulty is a real one and has coloured much of the literature, individual bias accounting for the conflicting statements as to the relative frequency of the two groups. Turning to recent papers, Tanner found 62 per cent of 101 tumours to be germinal carcinoma, while Bulkeley[8] regarded 40 out of his 59 cases as sarcomatous. Nicholson is much nearer the mark with 25 carcinomata (germinal) to 7 sarcomata (or 8, if including one beginning in the epididymis). I would draw attention to the fact that all the germinal tumours described and figured in this series, with one exception, have come to me from a variety of sources with the attached diagnosis of round-celled sarcoma, and it is impossible not to assume that there must be some sound reason for such unanimity.

Definition of Carcino-sarcoma.—This term is applied to certain tumours in which carcinomatous and sarcomatous features are blended. The *cells* in most are of an epithelioid character, but sometimes are of the large round, less often small round, oval, or coarsely spindle type so suggestive of sarcoma. In some cases an appearance of a firm granular or reticular matrix can be seen between the individual cells, even when these are typically epithelial, but it should be noted that this appearance is often seen in the cells of the seminiferous tubules. The *blood-vessels* may be of a mixed type in the same tumour. Well-formed or even thickened vessels often predominate, but may be associated in other parts of the growth with vessels of an embryonic type formed of a thin layer of endothelial cells set end-to-end, though the vascular chinks appearing between the individual tumour cells so characteristic of sarcoma are not often seen.

It is not uncommon to see in definitely carcinomatous tumours a patchy degeneration, areas of well nourished, deeply staining neoplastic cells alternating with degenerated, granular, poorly staining tissue. These appearances suggest that the tissue furthest removed from the vascular supply degenerates from deficient nutrition, for the deeply stained tissue is often aggregated in the form of nodules around thin-walled vessels. This appearance has been

described as angio-sarcomatous, but certainly occurs in undoubted carcinoma. In other tumours of the papillary adenocarcinomatous type a spurious peritheliomatous appearance may be produced by cross-section of the papillæ if they possess a highly vascular core.

The most reasonable explanation of these combined characters as observed in the germinal tumours is supplied by the *mesothelial* origin of the secreting elements of the testis. If we turn, for example, to the adrenal we find a parallel, for the adrenal cortex is developed from mesothelium. Certain cortical adrenal neoplasms may display sarcomatous features, though in the main the acquired epithelial characters predominate. Adami[9] has coined the term 'mesothelioma' for tumours derived from mesothelial structures, and as such structures play a dominant rôle in the development of the body of the testis we may reasonably expect to find some tumours displaying combined carcino-sarcomatous features, although, as in the adrenal, the acquired epithelial characters usually predominate.

So far as the evidence of metastasis goes, some tumours probably spread both by the blood- and lymph-streams. In two personally observed cases of carcinoma exhibiting partial sarcomatous features, metastasis involved both the lumbar glands and the liver. The majority of cases, however, behave as cancers, and metastasis usually first involves the lumbar lymphatic glands, though it is interesting to note that the traditional sarcoma testis, like round-celled sarcoma (?) of the thyroid, has in the past been credited with a special tendency to spread by the lymphatics.

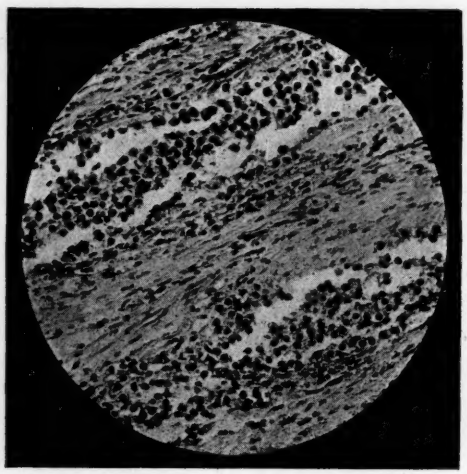


FIG. 218.—*Specimen* 5. Shows recognizable seminiferous tubules persisting in one area of the tumour.

The following two specimens are described as examples of carcino-sarcoma. They are essentially germinal-celled tumours in which sarcomatous characters are accentuated, and differ only in degree from the tumours previously described :—

Specimen 5.—(Labelled round-celled sarcoma.) The tumour was removed from a man, age 46, who for three years had noticed gradual enlargement of the testicle. The inguinal glands on the same side were involved, and there was also a mass in the lumbar region. Castration was performed to relieve the patient of the pain and discomfort caused by the weight of the tumour.

MACROSCOPIC.—The specimen is bisected and is roughly the size of an ostrich's egg. The cut surface is distinctly lobulated. The greater part of the tissue in the lower two-thirds has the appearance of being encapsulated, is split into lobules by fibrous septa, and shows hæmorrhagic infiltration and several patches of softening and others of pale degenerated tissue. The tissue forming the upper third is firm and more homogeneous. The epididymis is fused with the tumour.

MICROSCOPIC (*Figs.* 218, 219, 220).—The structure is that of a germinal carcinoma, but certain areas are so distinctly sarcomatous in type as to justify the

existing diagnosis. The cancerous areas appear both in the scirrhous and encephaloid form, and the cells are definitely germinal in type.

Sarcomatous features are evidenced by (*a*) round-celled characters—spindle in some areas, (*b*) embryonic blood-vessels and hæmorrhagic infiltration, (*c*) intercellular matrix. The inguinal glands show marked invasion, also of mixed character.

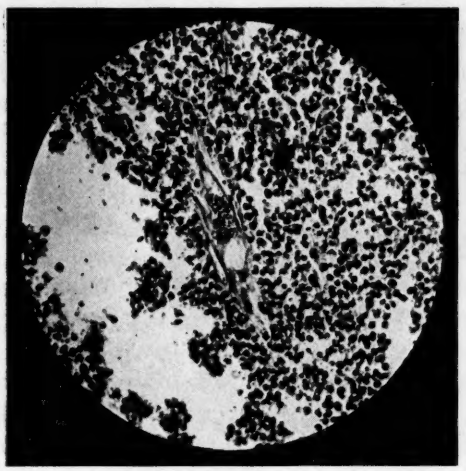


FIG. 219.—Same specimen, showing round-celled structure and thin-walled vessel.

FIG. 220.—Same specimen, showing mixture of round and spindle cells.

Comment.—This particular tumour, derived undoubtedly from germinal cells, exhibits a structure which may with justification be described as carcinomatous or sarcomatous according to individual bias. I regard it as a carcinoma arising from germinal cells, but exhibiting marked sarcomatous tendencies. Such a tumour can only arise from cells which possess both epithelial and mesoblastic potentialities, and the mesothelial tissue from which the secreting cells of the testis develops is the only likely source.

There is *metastatic invasion* both of the inguinal and lumbar glands, which serves to indicate the predominantly carcinomatous character of the tumour.

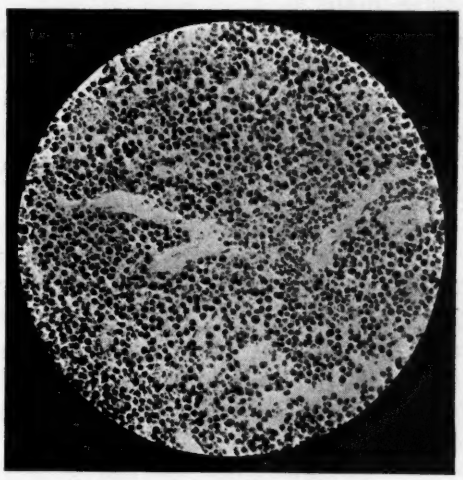


FIG. 221.—*Specimen* 6. Shows round-celled structure and capillaries lined by thin spindle cells. The tumour is old, and the cells are not so large as in the previous recent specimen.

Specimen 6.—(Labelled round-celled sarcoma.) The specimen comprising the testicular tumour, spermatic cord, and associated mass of lumbar glands was obtained post mortem, and the age of the patient is not stated. In addition to the lumbar metastasis there were also secondary deposits in the liver.

MACROSCOPIC.—The testicular tumour resembles the previous specimen in

size, and, as in it, the cut surface is divided into a lower lobulated area undergoing cystic degeneration and an upper solid area. The epididymis is incorporated.

MICROSCOPIC (*Fig.* 221).—

Testis.—The structure is that of the specific germinal tumour and is partly alveolar and partly encephaloid. Parts of the tumour are decidedly sarcomatous, if importance is to be attached to embryonic blood-vessels and to spindle-celled areas.

Lumbar Glands.—These are almost entirely replaced by neoplastic tissue displaying the same mixed characters. The hepatic deposits are not available.

Comment.—The tumour is of the germinal-celled variety, but, as with the previous specimen, there is good reason for the existing diagnosis. The metastases in the liver possibly stand interpretation as evidencing a blood-spread, in which case both elements of the tumour have produced metastases.

GENERAL CONSIDERATIONS.

Certain points arise for consideration out of the preceding examples, always remembering the danger of drawing inferences from comparatively few cases.

1. **The Age of the Patient.**—With only one exception these data are available, and the ages range from 39 to 52 years, with an average of 45. Nicholson, who accepted a germinal origin for his 25 carcinomata, found the average age incidence to be 43 years, and Schultz and Eisendrath[10] give it as 42·6 for the spermatocytoma group. These figures correspond closely, and we are justified in assuming that the specific germinal tumour develops most commonly in the forties, or in middle life, just when proliferative changes in, e.g., the mammary epithelium manifest themselves. At the same time it should be remembered that carcinoma of teratoid origin is also apt to declare itself in the same decade.

2. **The Duration of the Tumour.**—Reference to the quoted histories makes it clear that enlargement of the testicle had been noticed for a comparatively long time—three years in two cases and two years in two others. For what it is worth the inference here seems obvious that the specific germinal tumour is apt to be slow-growing. In three years *Specimen* 2 had only reached the size of the closed fist, and in two years *Specimen* 3 had only reached the size of an orange.

The teratoid carcinoma, on the other hand, arising in the fourth (or any other) decade, advances much more rapidly. Two examples will suffice to illustrate this point. The first reached the size of a small melon in six months and had already invaded the inguinal glands. The second attained the size of the closed fist in four months and had already fungated through the scrotum and invaded the inguinal glands. In each case the epididymis was fused and indistinguishable.

3. **Involvement of the Epididymis.**—French writers, Jeanbrau[11] for example, state that the epididymis long remains free in spermatocytoma. This is certainly true of the smaller examples (*Specimens* 3 and 4), but when a tumour is of long duration and has attained a large size it usually invades and incorporates the epididymis. Whether the epididymis remains free or not seems to depend partly on the site of origin of the tumour process in the body of the testis, and partly on its duration. If the blastomatous process

begins in or near the rete, as is usually stated, it naturally would be likely soon to infiltrate the adjacent epididymis, but with a more central origin the epididymis would probably escape till late in the disease (*Specimen* 2, of three years' duration).

4. **Macroscopic Appearances.**—The germinal tumours are typically solid, and the cut surface firm, fleshy, and homogeneous except for occasional whitish areas indicating patchy degeneration. The cut surface is often traversed by fibrous septa producing distinct lobulation, and sometimes imparting lobulation to the surface of the tumour. Occasionally softening and cystic degeneration may be present, but they are late developments.

5. **Microscopic Appearances.**—These may be considered under the following heads :—

a. Characters and Variations of Cells.—It is reasonable to expect that the influence of the blastomatous process may produce variations from the absolutely typical seminiferous cell, and this probably accounts for the fact that some germinal tumours are predominantly composed of large cells with a clear cytoplasm of the spermatocyte type, while others are composed of smaller cells with large darkly staining nuclei and much less cytoplasm, while in others again the cells may appear in parts of a remarkably large, rounded, polygonal, or pyriform type. The mesothelial origin of the germinal cell supplies sound reason for individual variations, and I am inclined to believe that reversionary tendencies play a large part in the production of the so-called lymphosarcoma testis. All through this group, as described previously, it is impossible to ignore the fact that we are dealing with cells which in some areas of the same tumour may be predominantly epithelial and in others sarcomatous, and if we allow full scope to these two potentialities we may reasonably expect, and do find, tumours ranging from adeno- or adenopapillary carcinoma down to others composed of small round cells hardly, if at all, distinguishable from lymphosarcoma, yet all arising from germinal cells.

The germinal cells, when lying loosely as seen in thin sections, are clear cut and free from any intercellular matrix. When closely packed, as in encephaloid patches, the cells tend to become polyhedral from mutual pressure and assume a mosaic appearance, and a fine granular or even reticular matrix appears between them. This appearance, however, is commonly observed in normal seminiferous tubules, and I am not inclined to attach much importance to it as evidencing sarcomatous tendencies, but regard it as a degeneration product thrown out from the cells under pressure.

It is an interesting feature in some of these tumours that many of the cells are strongly eosinophil. Southam and Linnell mention this point as supporting carcinoma, and it has been observed in several of the present series. It may be noted that in some control sections of normal testes the cells of the seminiferous tubules have been noticeably acidophil.

b. Arrangement of Cells.—In the early stages of the tumour, and sometimes even in the advanced, the tubular or alveolar arrangement is often preserved, so that portions of the spermatocytoma may differ from normal testicular substance only in a greater germinal-cell content and a corresponding reduction in the supporting stroma. Depending on the way in which the

tubules are cut, a markedly alveolar arrangement may predominate or the germinal cells may appear in closely-packed parallel sheets, separated by vessels enclosed in a scanty stroma, reminiscent of the adrenal cortex. In advanced stages and in rapidly growing tumours all alveolar arrangement may be lost except in scanty patches, and a predominantly encephaloid appearance results.

c. Retrogressive Tendencies.—These are occasionally observed in areas of these tumours. The connective-tissue stroma appears to gain the upper hand, and as it grows strangles the germinal cells, which become smaller, irregular, and granular.

d. Type of Blood-vessels.—It is stated that the blood-vessels in the specific germinal tumour are well formed and typical of carcinoma generally. This is true up to a point, but does not go far enough. In early cases the vessels are well formed in the main, but it is nearly always possible by repeated sections to find areas in which they are embryonal in type, and in other cases they may be typically sarcomatous. Consequently, too much stress should not be laid on the blood-vessel type in the diagnosis of seminoma or spermatocytoma, and, furthermore, these vascular peculiarities are likely to lead one astray in the interpretation of the small round-celled type of tumour resembling lymphosarcoma.

e. Lymphoid Stroma.—Chevassu describes a lymphoid stroma as a feature of the seminoma, and Ewing of embryonal carcinoma. All stages of its formation may be traced in the present group. In the beginning the lymphocytes appear along the lines of the vessels in the scanty stroma, and gradually accumulate and proliferate as the stroma and contained vessels disappear from the picture. Ultimately the lymphocytes come to form an interlacing network enclosing individual alveoli or groups of alveoli. This peculiar condition, I think, is best regarded as a connective-tissue reaction which seeks to confine the activities of the tumour cells—on the same lines, for example, as the round-celled barrier opposing the downward growth of the epithelial cells in a cancer of the lip or tongue.

In addition to, or apart from, a scanty or abundant lymphoid stroma, it is not uncommon to see nodules of lymph corpuscles scattered irregularly through the tumour tissue.

Heterologous Elements.—None appear in the various sections examined from the tumours of this group, but it must be freely admitted in fairness to the teratoid theory that an elaborate examination to exclude their possible existence has not been attempted. At the same time my experience has been that with the teratoid group piecemeal examination of different areas of a tumour invariably reveals its teratoid nature. Allowing for the imperfections in the methods of examination, it seems reasonable to conclude that those tumours are homologous, and arise from the germinal cells of the seminiferous tubules.

Choice of a Name.—The term 'spermatocytoma' which has recently come to be widely applied to these tumours of germinal-cell origin is open to objection. It implies a tumour composed essentially of cells resembling spermatocytes, i.e., large rounded cells with a big darkly staining nucleus and a considerable amount of clear cytoplasm. Some germinal tumours fulfil this

condition, but others do not and are composed of much smaller cells, and in others again the cells may assume giant proportions. All these are more probably variations from the germinal cell arising at some phase of the sexual cycle.

Chevassu's choice of term, ' séminome ', already anglicized to ' seminoma ', is preferable, because it only implies an origin from seminal cells and leaves more latitude. In many respects these tumours would be most accurately described under the heading of ' mesothelioma ' to indicate their fundamental origin and their frequently combined carcinomatous and sarcomatous characters, but this term is not likely to gain popular acceptance. Short of it, seminoma is the best and most comprehensive term, and allows scope for individual cell variations.

CONCLUSIONS.

1. The seminoma or germinal-celled tumour is one of the two common neoplasms of the testis, the other being the teratoma and its many variations, discussed in a previous communication.

2. *Origin.*—It arises from a proliferation of the cells of the seminiferous tubules in precisely the same way as glandular carcinoma of other organs.

3. *Age Incidence.*—It declares itself most frequently in the fourth decade.

4. *Rate of Growth.*—It advances more slowly than teratoid carcinoma.

5. *Structure.*—It presents in the main a specific structure which may be definitely related to the seminiferous cells, but is subject to certain variations in type.

6. *Carcinoma or Sarcoma?*—Carcinomatous features usually prevail, but it is common to find mixed histological characters in the same tumour. This feature is probably related to the mesothelial origin of the seminal cells and to reversionary tendencies.

7. *Metastases.*—Most germinal-celled tumours behave like cancer and spread by the lymphatics. Occasional spread by the blood-stream is to be related to sarcomatous characters.

The photographic work has been done by Mr. Frank Pettigrew, Technical Assistant to the Department of Surgery, to whom I am greatly indebted for his skill and care.

REFERENCES.

[1] Curling, *Med.-Chir. Trans.*, London, 1854.
[2] Chevassu, *Tumeurs du Testicule*, Paris, 1906.
[3] Debernardi, *Ziegler's Beitr. z. path. Anat.*, 40.
[4] Nicholson, " New Growths of the Testicle ", *Guy's Hosp. Rep.*, 1907, lxi.
[5] Tanner, *Surg. Gyn. and Obst.*, 1919, xxviii.
[6] Southam and Linnell, *Brit. Jour. Surg.*, 1923, Oct.
[7] Ewing, *Neoplastic Diseases*, 2nd edit.
[8] Bulkeley, *Surg. Gynecol. and Obst.*, 1922, xxxv.
[9] Adami and McCrae, *Textbook of Pathology*, 2nd edit., 393 and 739.
[10] Schultz and Eisendrath, *Arch. of Surg.*, 1921, May, ii.
[11] Jeanbrau, *Précis de Path. chir.*, iii.

LYMPHATICOSTOMY FOR PERITONITIS.*

By C. HAMILTON WHITEFORD, Plymouth.

Lymphaticostomy is the operation of exposing and draining the cervical portion of the left thoracic duct. The operation aims at diverting from the blood-stream bacteria and toxins absorbed from inflamed peritoneum and intestines, and was performed for the first time for peritonitis by Costain, of Toronto, in October, 1922.

ANATOMY OF THE THORACIC DUCT.

The anatomy of the cervical portion of the duct varies greatly. Wyllys Andrews[1] states that the duct may be double or even triple. The right duct may be equal to, or more developed than, the left. The duct may enter the subclavian vein by two or three branches, or may enter a vein other than the subclavian. Regarding the relative frequency of these variations, Wyllys Andrews[2] quotes the results of several series of dissections. In one series of 40 cases, in 18 the duct had two branches, and in 9 of these 18 the duct re-united; 7 had two insertions into the vein, and 2 had four insertions. In another series of 24, the duct was branched in 6. In a third series of 17, the duct was branched in 8. Gerrish[3] considers that "The size of its terminal portion depends upon the presence or absence of branches given off to the veins as it rises through the thorax".

Costain[15] supplies the following details: "There is a suction force on the thoracic duct, due to the venous blood passing the opening of the duct, similar to that created by the Sprengel pump. In lymphaticostomy the ligature cuts off this suction, and when the duct is opened there is a flow of lymph. The duct does not become distended when ligated, and the lymph-flow is less than one would expect from observing the flow through the duct before ligaturing and opening. [If this suction is the chief cause of the lymph entering the vein, the profuse discharge, recorded in cases of lymphaticostomy with ligation of the duct, ought not to occur. Probably the respiratory movements are an equally important factor.—C. H. W.] The normal duct is transparent, its contents being visible. In peritonitis, however, the fluid may be bloody, and the duct may resemble a vein, and must then be distinguished by its position."

The difficulty of finding the duct in the cadaver is due to the fact that the duct is collapsed, and in that condition resembles fibrous tissue. It is more difficult to find in the dog than in man.

---

* A paper read before the Plymouth Medical Society, March 17, 1925.

EXPERIMENTS.

Costain[4] produced in dogs a septic peritonitis which, when untreated, proved fatal in about forty-eight hours. Ligation and drainage of the thoracic duct performed during the first twenty-four hours (without drainage of the peritoneal cavity) saved many of the dogs.

Williamson and Brown,[5] in the Mayo Clinic, carried out experiments on dogs in order to decide whether passage of bacteria from the abdomen to the lungs, via the thoracic duct, was a cause of pneumonia following abdominal operations. They employed the *Bacillus prodigiosus* as being not normally found in the alimentary canal, non-pathogenic, and easily identified. With the thoracic duct opened, bacteria, either swallowed or injected into the jejunum or into the colon, were never obtained from the duct; but bacteria injected into the peritoneal cavity appeared in lymph from the duct two to four hours after injection, in 4 out of 8 cases.

CLINICAL CASES.

In conditions other than peritonitis the duct has been opened in the neck: (1) For fat embolism by Wilms[6]; the divided duct drained freely and closed after six days; the patient recovered. (2) In the course of operations in the supraclavicular area; Fredet[7] collected 58 such cases, and of these only 5 died; the majority of the cases, when the fistula did not close spontaneously, were treated either by ligation of the duct or by compression. (3) By accidental (non-operative) injury. (4) In cases of abdominal cancer (Jonnesco[8]).

Recorded cases of human peritonitis treated by lymphaticostomy are few in number, and being widely scattered throughout surgical literature are difficult to trace. The following list of such cases has been collected, but makes no claim to completeness.

Case 1 (Costain[9]).—Pneumococcal peritonitis, in a girl, age 9. The abdomen was not operated upon, but the patient was exsanguinated and transfused. Pneumococci (Type IV) were found in pus aspirated from the abdomen. No bacteria were found in the blood or in the lymph, which was not tested for toxicity. Toxic symptoms rapidly disappeared. Drainage from the duct, at first free, ceased on the seventh day. On the twentieth day after operation the patient was discharged cured.

Costain's Technique.—A three-inch incision is made along the lower posterior border of the left sternomastoid muscle. Blunt dissection exposes the sternomastoid muscle, which is drawn forwards, and the omohyoid muscle, which is drawn upwards and backwards. The internal jugular vein, exposed down to its junction with the subclavian vein, is rolled forwards, exposing the thoracic duct. The duct is ligated with catgut close to its termination, and a half-inch incision is made in the long axis of the duct above the ligature. A narrow strand of rubber is passed into the duct. The operation is performed under either general anæsthesia or local infiltration.

Following Costain's lead, other surgeons have performed lymphaticostomy for peritonitis.

Case 2 (Edwards[10]).—Puerperal pneumococcic peritonitis. The patient, age 17, was operated upon thirty days after confinement, under novocain anæsthesia. On the third day improvement in the abdominal and general condition was marked and sustained. The wound healed by granulation, and the patient was discharged cured fifty-one days after operation. Glucose was given intravenously both before and after operation. Transfusion of citrated blood was performed on the day before operation. Blood cultures were negative, but the fluid from the duct contained pneumococci. Drainage from the duct was free during the first three days, and ceased on the eighth day.

Case 3 (De Lee[11]).—Puerperal peritonitis and septicæmia in a primipara, age 25. The primary septic focus was in the perineum, whence the infection spread to the peritoneum and blood-stream. Streptococci were found in the blood in pure culture. Under local anæsthesia, the patient being nearly comatose, the duct, which entered the internal jugular vein, was found with some difficulty and was drained. "Within half an hour the patient's mind cleared up, and she sat up and demanded food. In about eight hours, however, coma returned, and she died the next morning". The fluid from the duct was profuse but sterile. No operation was performed upon the abdomen.

Case 4 (Cooke[12]).—A man, age 48; septic peritonitis, treated by removal of a perforated appendix, the abdomen being closed without drainage. Lymphaticostomy was performed immediately after the cœliotomy. "The duct was ligatured off from the vein, slit up, and stitched to the skin". After a stormy convalescence, the patient was discharged cured, twenty-five days after operation. The duct was hard to identify, being "delicate in texture and thinner than one expects". Beads of lymph were visible in the unopened duct. The patient having been dehydrated by vomiting and starvation, the flow of lymph became free only after twenty-four hours of continuous rectal saline.

Case 5 (D. A. Mitchell[13]).—A briefly recorded case of "ruptured intestine" of sixty hours' duration, with loss of liver dullness. After lymphaticostomy the patient lived twenty-four hours, during which time the duct drained freely. The difficulty of the operation lay in having to work "practically behind the clavicle".

Case 6 (Alexander Mitchell[14]).—Pneumococcal peritonitis in a girl, age 4 years. Cœliotomy evacuated a large amount of pus. A drainage tube was passed into the pelvis through the lower angle of the incision. Improvement, local and general, followed, and lasted for a week. Then the abdomen again became distended and painful, with rise of temperature and pulse. Lymphaticostomy was performed fourteen days after the cœliotomy. Lymph drained freely, with general and local improvement for five days. Then, "although the abdominal condition appeared to be most satisfactory, and the child was taking abundant nourishment by the mouth, she seemed to be getting weaker and to be losing weight rapidly". A free flow of lymph continued up to shortly before death, which occurred nine days after the lymphaticostomy. Pneumococci (Type II) were found in the abdominal pus. No organisms were found in the lymph.

Mitchell says: "From observation of this case alone, the impression was that the lymphaticostomy had a remarkably beneficial effect on the course of the peritonitis, but that it seemed highly probable that the continuous discharge of lymph from the thoracic duct was the ultimate determining cause of the patient's death." Also: "The main difficulty seems to me to be, what is going to happen to the patient if his duct fistula does not heal when his abdominal condition improves. If the discharge of lymph continues for more than a few days; it is obvious that the loss of the essential food constituents must be a very serious matter." He asks for Costain's opinion as

to what happens when the fistula ceases to discharge, and whether it is possible that the ligature on the duct is absorbed and circulation through the duct resumed.

Case 7 (Costain[15]).—A second case of recovery, in a boy, age 10 years, who, after four days' illness, had cœliotomy performed, disclosing a ruptured appendix and diffuse peritonitis. The appendix was removed, with drainage both of the peritoneum and the terminal ileum. On the day after the cœliotomy, since he was going downhill, lymphaticostomy was performed under gas and oxygen. A strand of silkworm gut was passed down the duct for about 1 in., a rubber tube being threaded over the silkworm gut down to the duct. No mention is made of ligation of the duct close to the vein. No bacteriological findings are given. The flow of lymph was profuse for forty-eight hours and had ceased by the fifth day. The tube and silkworm gut were removed on the second day. Recovery was complete.

Mackenzie[16] has performed lymphaticostomy twice, but does not give details or results. He mentions the technical difficulties in identifying the duct on account of its small size and thinness, and of inserting and retaining the rubber drain in the duct. To overcome the latter difficulty he advocates, but has not tried, a tapering cannula with a bulbous tip which is retained in the duct by a fine catgut ligature. The cannula, being made of silver, can be bent to fit the wound.

The writer has knowledge of two other cases (not yet published) of peritonitis treated by lymphaticostomy. Both died.

COMMENTS.

In the above collection of 11 cases, details are available in 7, with 3 deaths and 4 recoveries (*Cases* 1, 2, 4, 7). In 3 cases the infection was pneumococcal, and of these, 2 (*Cases* 1 and 2) recovered. In none of the 7 cases is there a record of examination of the lymph for toxicity. Such examination is especially called for when the lymph is found to be sterile. The effect of the lymphaticostomy on the peritonitis is difficult to estimate, especially when, as in some of the cases, the peritonitis has been treated by cœliotomy. But it is to be noted that the peritonitis was not treated by abdominal operation either in Costain's experiments on dogs, or in *Cases* 1 and 2, which recovered. Equally difficult is it to say, in regard to the cases which died (except in *Case* 6), whether, or to what extent, the lymphaticostomy contributed to the fatal termination. Excluding the pneumococcic patients, the cases which died without drainage of the abdomen raise the question whether the omission of drainage did not deprive these patients of a possible chance of survival. The amount and duration of the lymph-flow from a partially or totally divided thoracic duct probably depends largely upon the anatomical arrangement of the lymphatic system.

In any given case of lymphaticostomy, and in cases of fistula following unintentional surgical injury or accidental trauma, it is usually impossible to say whether the duct consists of a single trunk or of several branches, while except in lymphaticostomy it is known only rarely whether the duct has been partly or completely divided.

In cases which survive, with closure of the fistula, there are three possible

routes for the chyle, which may reach the blood-stream by: (1) Other branches existing in the left side of the neck; (2) The right duct or thoracic veins, by enlargement of branches of communication within the thorax; (3) Its original course, the injured duct undergoing repair; and (4) Any combination of these three routes. In regard to route 3, it is known that, throughout the body, small ducts, even when tightly ligated, occasionally manage to re-establish their lumina, but such restoration of the lumen takes time and cannot be relied on. Also, it is a clinical fact that a small duct incised in its long axis has a strong natural tendency to heal without serious stricture, provided there is no complete obstruction of its lumen.

In lymphaticostomy, since there is always the possibility that the duct which is drained may be the chief route for the chyle, a permanent obliteration of the lumen, either by tight ligation or transverse division, involves the risk of depriving the patient of a large amount of nutriment. An operation which (as in *Case* 6) rescues the patient from peritonitis, only to kill him by starvation, is lamentable. Preservation of the lumen of the duct would provide a definite chance of some, at least, of the chyle reaching the blood-stream by its accustomed channel.

It appears desirable to provide during the lymphaticostomy: (1) For preservation of the lumen of the duct; (2) A simple method of stopping, at any given moment and without further operation, the escape of chyle from the fistula. The writer ventures to suggest that these two ends might be attained by the following modification of Costain's technique. For a large duct, employ the cannula suggested by Mackenzie. The larger the duct, the less difficult its intubation and the greater the probability that the duct is the chief route for the chyle. The cannula is advocated, not so much on account of difficulty in inserting the rubber drain (Mackenzie's reason for using the cannula), as because the cannula renders superfluous the ligature on the duct close to the vein. The bulbous tip of the cannula is retained in the duct by a catgut ligature tied as the first half of a surgical knot, the ends being left long. The catgut, hardened to resist absorption, must not be so fine as to cut easily into the duct walls. For removal of the cannula, the knot is loosened and the ligature is left *in situ*, encircling the duct. Should the discharge from the fistula continue for so long a time, or in such an amount, as to endanger the patient's nutrition, the escape of chyle can be stopped by tightening the ligatures. Should the fistula close spontaneously, the ligature can be easily removed. If experience proves that the segment of duct compressed between the ligature and the cannula tends to become necrosed, an extra ligature placed loosely round the duct above the cannula during the lymphaticostomy will provide a means of closing the fistula.

When the duct is too small for intubation, a loop or strand of silkworm gut takes the place of the cannula, and two ligatures similar to that previously described are placed loosely round the duct on each side of the fistula. The distal ligature is tightened only when the flow from the fistula is so slight as to suggest that an appreciable amount of lymph is still flowing past the fistula into the vein. The proximal ligature provides for stopping the flow from the fistula. The ligatures, when no longer required, can be removed by loosening their half-knots.

Proximal ligation of the duct, although stopping the external loss of chyle, does not necessarily imply an *immediate* restoration to the blood-stream of an amount of chyle equal to that which has been escaping from the fistula. The amount of chyle returned *at once* to the circulation depends largely on whether competent accessory lymph-channels already exist or have to be developed. This, in any given case, is an unknown factor. The records of accidental injuries to the duct which healed without ligation suggest that the omission of the ligature on the duct between the fistula and the vein entails only a theoretical risk of air entering the vein via the fistula.

INDICATIONS FOR LYMPHATICOSTOMY.

Costain[15] says: "The indications for the operation are not yet clear", and that surgeons are not unanimous in accepting the theory that most of the post-operative symptoms regarded as complications are due to septic absorption. He considers the operation to be indicated in :—

1. Secondary peritonitis, as in Cooke's case (*Case* 4), as an adjunct to dealing with the condition locally. In some cases cœliotomy and lymphaticostomy have to be done simultaneously. [In regard to *Case* 4, advocates of drainage will argue, not unfairly, that drainage of the peritoneal cavity might have obviated the lymphaticostomy.—C. H. W.]

2. In all cases in which, after the abdominal operation, symptoms of continued septic absorption persist. Lymphaticostomy should not be delayed until the patient's condition is hopeless.

3. "In primary peritonitis, especially the pneumococcic, in which the diagnosis is clearly established." "When the diagnosis is doubtful, the abdomen should be opened first, in order to verify the condition".

Costain says in conclusion: "I believe that, with good judgement in election and skill in the performance, lymphaticostomy will lower the mortality rate in diffuse peritonitis, by saving those to whom relief could not otherwise come".

CONCLUSIONS.

1. No general agreement has, as yet, been arrived at on the indications for lymphaticostomy.

2. The experimental and clinical evidence at present available suggests that a further trial of lymphaticostomy is desirable.

3. Much more clinical experience of lymphaticostomy must accumulate before the value and risks of the operation can be decided.

4. Identification of the duct may be difficult. In at least 30 per cent of cases (nearly 40 per cent in the combined series quoted by Wyllys Andrews) the operator must be prepared to find a duct which does not consist of a large single trunk opening into the subclavian vein.

5. In recorded cases in which the escaping lymph was sterile, the toxicity of the lymph appears to have been taken for granted. In records of future cases, proof of such toxicity should be given.

6. Permanent or prolonged obliteration of the lumen of the duct, by complete division or by ligature, appears to accentuate unnecessarily the risk

of a flow from the fistula so persistent and profuse that death occurs from starvation. Preservation of the lumen might give the chyle a chance of resuming, in part at least, its original route. Provision should be made during the performance of lymphaticostomy for stopping the loss of chyle without having to perform a further operation on a debilitated patient. A technique which may accomplish this is described.

Since the above was in type, the two following papers have appeared.

H. H. Cox and L. B. Bell[17] experimented with dogs on lines very similar to those of Costain, but failed to confirm Costain's findings. They consider that the current of lymph is maintained by respiration, each inspiration producing within the thorax a temporary negative pressure which withdraws chyle from the abdomen. Fistulous drainage appeared to hasten the death of the animal, probably by starvation. Ligation of the thoracic duct prolonged the lives of the dogs, probably by retarding absorption of toxins. "Suspended carmine particles and methylene blue were injected into the free peritoneal cavity, and in two cases appeared in the chyle from the thoracic duct within five minutes. In two other cases it did not appear within forty-five minutes. The results indicate that the rate of absorption through the thoracic duct is by no means constant."

L. D. McGuire[18] conducted in the Mayo Clinic experiments with *B. prodigiosus* in peritonitic dogs. He found that: (1) *B. prodigiosus* was never found in lymph from the thoracic duct; (2) The toxicity of the lymph from the duct, tested by intravenous injection into rabbits, was practically nil; (3) Peritonitis in dogs was not benefited by lymphaticostomy. McGuire's results differ from those of Williamson and Brown[5] in the Mayo Clinic.

REFERENCES.

[1] Andrews, Wyllys E., *Keen's Surgery*, iii, 314.
[2] Andrews, Wyllys E., *Ibid.*, vi, 321.
[3] Gerrish, F. H., *Ibid.*, ii, 585.
[4] Costain, W. A., *Jour. Canad. Med. Assoc.*, 1922, Nov.
[5] Williamson, C. S., and Brown, R. O., *Amer. Jour. Med. Sci.*, 1923, April, No. 4, clxv, 480.
[6] Wilms, *Sémaine méd.*, 1910, March 23.
[7] Fredet, *Presse méd.*, 1910, Jan. 1.
[8] Jonnesco, quoted by Murphy, J. B., *General Surgery*, 1911, ii, 272.
[9] Costain, W. A., *Surg. Gynecol. and Obst.*, 1923, March, 365.
[10] Edwards, A. E., *Ibid.*, 1924, Feb., 256.
[11] De Lee, J. B., *Ibid.*, 1925, Feb., 297.
[12] Cooke, A., *Brit. Med. Jour.*, 1924, i, 1098.
[13] Mitchell, D. A., *Ibid.*, ii, 36.
[14] Mitchell, Alexander, *Ibid.*, 214.
[15] Costain, W. A., *Ibid.*, 857.
[16] Mackenzie, C., *Ibid.*, i, 1114.
[17] Cox, H. H., and Bell, L. B., *Ann. of Surg.*, 1925, May, 911.
[18] McGuire, L. D., *Surg. Gynecol. and Obst.*, 1925, May, 626.

LYMPHATICOSTOMY IN PERITONITIS.

By ARTHUR COOKE, Cambridge.

The efforts of general surgeons to reduce the mortality from acute general peritonitis have been crowned with so much success during the last twenty-five years that we are apt to put the matter aside as sufficiently dealt with by prompt emergent surgery. It is a platitude to say that success largely depends on early diagnosis, efficient transport, and effective surgery. Where one of these fails to function, from whatever cause, the fate of the inflammatory type, of acute abdomen as distinguished from the obstructive type is death from peritonitis in the majority of cases. No doubt other causes of death, too obvious to mention, play their part, but it will probably be generally conceded that acute general peritonitis is the most frequent.

On consulting the Registrar-General's Report for 1923, published in 1924, the following figures for England and Wales are of interest :—

Deaths from	appendicitis	2826
,, ,,	duodenal ulcer	907
,, ,,	gastric ulcer	2105
,, ,,	hernia	1738
,, ,,	biliary calculi	1030
,, ,,	peritonitis (cause unstated)	417
,, ,,	puerperal sepsis ..	985

In a previous year (1920) the deaths from gastric ulcer were classed as 'perforating ulcer of the stomach, 1975'. It is impossible to state with any degree of accuracy what number of deaths in the above list was caused by peritonitis, but a moderate estimate would probably be one half, or about 5000 : no excuse is necessary for recording cases which may point to a means of reducing that number.

Costain's[1] records of lymphaticostomy in dogs at the time of tying the appendix with the object of producing general peritonitis are as follows :—

7 dogs had appendix and mesentery tied, with no lymphaticostomy: all died in forty-eight hours of peritonitis.

11 dogs had appendix and mesentery tied, with simultaneous lymphaticostomy : 4 recovered, having developed thoracic duct fistula ; 7 died without developing fistula of thoracic duct.

7 dogs had appendix and mesentery tied, with lymphaticostomy twenty-four hours later : 3 recovered—all had duct fistula ; 3 died with no fistula, there being collateral flow of lymph ; 1 died from pneumonia.

Assuming for the moment that lymphaticostomy is advantageous in peritonitis, the difficulty in human surgery is to decide when general peritonitis is of such severity as to demand this further operation in addition to removal

of the cause. To convey outside the body the main stream of lymph which is assumed to carry into the blood a considerable amount of the toxins absorbed from the peritoneum appears desirable. No one would advocate this remedy for a moribund patient; no one would think it necessary for an appendicitis of good prognosis with a moderate peritonitis likely to be controlled by the ordinary methods. Between these two extremes there is a fairly large class known to surgeons engaged in active emergency work where the mortality may be easily gauged as over 10 per cent.

The mode of death in general peritonitis requires consideration. Vomiting and stagnation of intestinal contents are prominent symptoms, but they would hardly cause death without the toxæmia which reduces the volume of the pulse and gives rise to the ashen grey colour of the face. The contrast of a patient with severe vomiting but no toxæmia may be studied in a case of vicious circle, where the pulse remains good in spite of persistent vomiting. I have notes of such a case which occurred in 1906. Again, stagnation in the alimentary tract with distention is usually overcome if there is no general peritonitis, and in most cases it does not produce the depression of toxæmia.

TECHNIQUE OF LYMPHATICOSTOMY.

A sand-bag or firm pad is placed under the upper dorsal spine, and the head drawn back and to the right. A 3-inch incision is made along the outer edge of the left sternomastoid in its lowest part: by retracting it inwards and the omohyoid outwards, and a careful blunt dissection, the junction of the internal jugular vein with the left subclavian vein is easily found and may be maintained in a perfectly dry condition. This dry condition is important for discovering that delicate structure, the thoracic duct. It is to be found entering the posterior surface of the subclavian vein either at or near its junction with the internal jugular vein: its size is no greater than a very small vein; its colour is yellow and it is nearly transparent. When found, its identity may be verified by putting a small pair of Spencer Wells on it close to its entry into the large vein. Under these conditions it fills with yellow transparent fluid in less than a minute. Its distal end is tied off and a fine glass cannula is passed into the slit-up duct, and this severed and attached to the skin by a stitch. Failing the use of a cannula, which I have not yet found small enough, the slit duct is stitched lightly to the edge of the wound.

The points to be remembered are: (1) A dry wound is necessary; (2) A light touch is needed in dissection, for as the duct is much more delicate than any other structure I have met with in general surgery; (3) The duct is nearly empty owing to depletion of the patient by starvation and vomiting.

Professor Langley has assured me that the way to find the thoracic duct in dogs is to give them a good meal of fats two hours before the operation. The directly opposite physiological conditions in a depleted patient make it necessary to have an assistant and a good light. In one case (*Case* 3) I believe I mistook the fine lymphatic trunk from the cervical glands for the main duct.

There are at least three points about this severance of the main lymphatic duct which require consideration: (1) The possibility of healing; (2) The

ultimate new path adopted by the lymph; (3) The presence of toxins in the lymph.

1. In the three cases where a complete severance of the duct is believed to have been made, the amount of lymph was not excessive, not more than 1 or 2 oz. a day. It diminished rapidly after the first few days, and the wound, which was left widely open at first, closed naturally in from two to three weeks without any fistula. Accidental lymphatic fistulæ have been cured by various means, Morgan, of Chicago,[2] adopting rectal feeding with success. This imitates the depletion found in patients suffering from peritonitis.

2. The ultimate new paths for the lymph are variously stated. Costain believes that the right lymphatic duct is the alternative path. Wendel[3] and V. C. Pennell (Cambridge School of Anatomy) state independently that an alternative lymph channel is to be found into the left azygos vein. Clinical evidence supports an alternative route: (*a*) *Case* 1 is in good health with no lymphatic œdema; (*b*) Patients who have had severe operations on the posterior triangle, or gunshot wounds with scarring, do not develop signs of lymphatic block.

3. The presence of toxins in the lymph must be accepted if Costain's figures for the operation in dogs are credited. In future cases it is my intention to collect the lymph by means of a cannula and obtain if possible direct evidence of its toxicity. So far, cultures from the lymph in these cases have proved sterile.

CASE REPORTS.

Case 1.—**Appendicitis with general peritonitis.**[4]

An agricultural labourer, age 48, was admitted to Addenbrooke's Hospital on April 15, 1924, with a history that on April 13 he awoke at 2 a.m., with severe abdominal pain. In spite of that he got up and milked the cows. His bowels acted, but he became progressively worse, with pain and vomiting, on April 14, and was admitted to hospital on the afternoon of April 15. At this time there was considerable distention of the abdomen, restricted respiratory movements, especially in the lower abdomen, surface hyperæsthesia in the left iliac region, and deep tenderness across the whole lower abdomen. Per rectum there was tenderness and a tense feeling in the pre-rectal pouch. Pulse 88, regular; temperature subnormal; tongue dry. A large fæcal vomit occurred just before I examined him. Unable to make any diagnosis other than 'acute abdomen', I opened in the middle line and inspected numerous coils of small intestine, all of which were acutely inflamed, distended, and deep scarlet in colour, with occasional slight smears of pus. The appendix was perforated; around it there were no local conditions other than those general to the middle and lower abdomen. The appendix was removed and the wound closed without drainage, the severe distention causing the usual difficulties in such cases of abdominal wall closure. Having decided that this was a case where recovery by the usual methods of after-treatment was almost out of the question, I proceeded to perform Costain's lymphaticostomy.

I exposed the junction of the internal jugular with the left subclavian vein, and identified the thoracic duct by its position and by seeing it fill with beads of brilliant clear yellow fluid resembling thin honey drained from the comb. The duct was ligatured off from the vein, slit up, and stitched to the skin; the wound was left open and lightly filled with gauze. A culture from this lymph was proved next day to be sterile.

On April 16 the patient was progressively more ill; he was semi-conscious at 10 a.m.; pulse irregular and feeble. There was only a small exudation from the wound in the neck. Abdomen still distended. At 11 p.m. he was still semi-conscious, could just be roused; chyle was discharging more freely from the neck. Respirations 28, pulse 128. The next day he was fully conscious, the pulse had improved, though the abdomen was still distended. Chyle was pouring freely from the neck, a dirty white colour.

April 19.—The distention was decreasing; good result at last after numerous enemas and six doses of pituitrin at intervals. The neck was still discharging freely. Pulse good.

April 23.—The distention had gone. There was discharge of pus from the abdominal wound and sudden diminution of chyle from the neck. By April 26 the neck was practically dry; the bowels acted daily. Since April 17 the temperature had never been above 98·8°.

May 10.—The patient was discharged from hospital with both wounds healed and normally convalescent.

Comment.—The paucity of lymph in the first twenty-four hours in this case is explained by the fact that this man was depleted of fluid by starvation and by a large fæcal vomit; it was only after continuous rectal saline for twenty-four hours that lymph began to flow freely. No measures were taken to stop the flow of lymph, and this subsided in a week.

A year later the man is in normal health.

Case 2.—**Puerperal septicæmia with general peritonitis.**

A. W., age 24, admitted under Dr. J. Campbell Canney on third day of septic puerperium after confinement (midwife), April 27, 1924. Pain in lower abdomen, vomiting, temperature 103·4°. Immediate local uterine treatment.

Fourteenth day: temperature has varied from 102° to 99°; left knee effusion; abdomen distended. Fifteenth day: abdomen more distended, temperature 101°, pulse 120. Dr. Canney called me in with a view to lymphaticostomy. The abdomen was enormously distended and tender, with no liver dullness.

Operation.—The thoracic duct was exposed, ligated distally, and the proximal part incised and sutured to the wound. The abdomen was opened; a large quantity of free gas and some pus escaped. A condition of general peritonitis with thin pus; culture, *B. proteus* and streptococcus. Rubber drain left in. Pus and gas continued to discharge, and on the twenty-second day, when the wound was opened up again, a fæcal fistula developed.

The lymphaticostomy hardly drained on the first day; more fluid discharged on the second day and for one week. The general condition appeared to improve somewhat after the lymphaticostomy and abdominal incision until the twenty-fifth day, when the respirations increased to 40 and 50, and the patient died on the thirty-second day with signs of pneumonia.

Case 3.—**Appendicitis with general peritonitis in a girl.**

J. D. A., age 4. Admitted Nov. 27, 1924, with a history of five days' illness, vomiting and abdominal pain.

On admission, pale, dusky complexion. Pulse ? 180, temperature 100·2°. Tongue coated with black fur (? bismuth). Abdomen very rigid, distended, tender all over, especially in right iliac fossa. Liver dullness diminished.

Operation.—Appendicectomy; appendix gangrenous. Generalized pus in abdomen. Tube drainage. Lymphaticostomy performed; the lymph duct severed was very small and never gave a satisfactory flow of lymph, although two or three drachms drained out daily for a few days. The child gradually improved and the temperature fell to normal in fourteen days. About the fifteenth day a secondary abscess discharged itself through the wound. The child left the hospital all healed on Jan. 8, 1925.

Comment.—The general severity of the case and high mortality in young children led me to perform what I believed at the time was a lymphaticostomy. The poor flow of lymph makes it more than likely that the lymph vessel from the cervical glands was opened.

Case 4.—**Appendicitis with general peritonitis.**

F. S., male, age 31. Onset with acute abdominal pain, April 16, 1925.

Admitted April 18, 1925. Patient collapsed, in great pain, with subnormal temperature. Board-like rigidity all over abdomen; pain referred chiefly to right iliac fossa.

OPERATION.—Right pararectal incision caused a large quantity of foul-smelling purulent fluid to escape; appendix completely gangrenous. All visible coils of intestine acutely inflamed with no closing off of purulent area. Tube drainage. Lymphaticostomy performed.

April 29.—There has been quite satisfactory drainage of lymph from the neck until to-day, when flow is only slight. Patient is now apparently making a good recovery, but temperature is 100·2° at night and at times there is distention of the abdomen. Per rectum a soft indefinite swelling.

May 2.—Patient feels very well and is able to read. Rather more swelling felt per rectum. 7.30 p.m.: sudden urgent dyspnœa and death from pulmonary embolism.

Comment.—This was a very severe case; toxæmia with board-like abdomen, unlikely to recover. The patient reached semi-convalescence, and death from pulmonary embolism on the fifteenth day after operation is no proof that the lymphaticostomy did not help him considerably. Possibly if the swelling in the pelvis, which was just palpable, had been drained, pulmonary embolism would not have occurred.

SUMMARY OF THE FOUR CASES.

1. Recovered, apparently as a result of lymphaticostomy.
2. Died of pneumonia and general exhaustion seventeen days after lymphaticostomy, which had produced some improvement.
3. Recovered in spite of lymphaticostomy only producing a slight flow of lymph.
4. Recovered from all acute symptoms, and when convalescent died on the fifteenth day of pulmonary embolism.

REFERENCES.

[1] *Canad. Med. Assoc. Jour.*, 1922, 789; *Surg. Gynecol. and Obst.*, 1923, March.
[2] *Keen's Surgery*, vi, 322.
[3] *Ibid.*, 236.
[4] *Brit. Med. Jour.*, 1924, June 14.

A CONSIDERATION OF THE HYPOPHYSIAL ADENOMATA.*

By NORMAN M. DOTT, Edinburgh, and PERCIVAL BAILEY, Boston.

With a Prefatory Note by HARVEY CUSHING, Boston.

PREFATORY NOTE.

It is highly profitable at times for a chief of service to play the part of bystander and to see what interpretations younger and fresher minds may put upon matters in which he perhaps has somewhat fixed ideas. In assembling for publication one's own familiar case histories, impressions and opinions may be read into them, albeit unconsciously. Those who peruse these histories for the first time, never having seen the majority of the patients, are at least spared from any such prejudices in their handling of the material.

On this basis, Mr. Dott and Dr. Bailey have made the accompanying review of the cases discharged from the Brigham Hospital Clinic with verified pituitary adenomata. They give some new interpretations of these lesions and arrive at some novel conclusions, particularly in their creation of a third or mixed type of adenoma with a corresponding clinical syndrome which shows a variable overlapping of the symptoms attributable on the one hand to hyperfunction and on the other to hypofunction.

Even without the tell-tale signs of tumour, there is no mistaking a definite case of acromegaly nor a definite example of pituitary insufficiency, but when we begin to split hairs over the intermediate clinical types which have been classified under the term dyspituitarism, we find ourselves in difficulties. We may see among these patients with pituitary adenomata overgrown individuals who are at the same time adipose and sexually dystrophic. On the other hand, as in one case the authors have chosen to report, we may see individuals who are skeletally undersized and yet show no genital dystrophy. Moreover, they may be either fat or lean. In short, we are dealing with a complicated matter affecting growth, metabolism, and sexual development in which there is undoubtedly some intimate interplay between hypophysis and gonads.

Since the publication of my monograph in 1912 there has been no general assembly of cases from the Clinic, and, as the authors say, it is probably wise at present to eliminate from discussion the many hypophysial disorders due to other than an actual glandular adenoma and to devote one's attention solely to the syndromes which accompany this particular lesion.

---

* From the Surgical Clinic of the Peter Bent Brigham Hospital, Boston, Massachusetts, U.S.A. Presented before the Surgical Section of the American Medical Association June 12, 1924.

It is somewhat disconcerting to realize how little advance in our knowledge of these disorders has been made during the past twelve years.

On the experimental side we have learned that extracts of the posterior lobe, contrary to the early interpretation of the physiologists, actually cause an oliguria rather than a polyuria, and this information has come to be applied in the treatment of diabetes insipidus. A somewhat academic discussion has arisen concerning the relation of diabetes insipidus to a lesion affecting the hypophysis versus one affecting certain adjacent nerve centres in the hypothalamus. But what is of greater importance, Evans has given the first experimental support to what has heretofore been merely an assumption—that the overgrowth which characterizes gigantism, and probably acromegaly as well, is, as long surmised, actually an expression of hyperpituitarism.

On the clinical side there has been a great improvement in cranial roentgenology, which has made it possible not only to have a better understanding of the deformities of the sella turcica, but also to detect, in many cases, the suprasellar tumours of congenital origin which arise from relics of Rathke's pouch and which in childhood produce the standard examples of so-called Frölich's syndrome. There has also been a great improvement in our operative procedures, a result of the surgeon's increased experience in exposing these lesions; but beyond these few things our progress in the twelve years has been slight. We are far from having any exact knowledge of the chemistry of pituitrin—still farther from any knowledge of the active principle (or principles) of the anterior lobe which influences growth. These objectives will be attained in due course, but there are many obstacles to surmount.

In the before-mentioned monograph, a parallel was drawn between these hypophysial disorders and corresponding thyroid disorders, and I do not know that we can do better to-day, for we are not entitled to base too much clinical importance on histological studies, even such precise ones as Dr. Bailey has made. It will be recalled that our understanding of exophthalmic goitre as a state of hyperthyroidism goes back to Halsted's studies of experimental thyroid hypertrophy, and that Halsted himself, after twenty years, was unable to repeat successfully his early experiments, and expressed himself as probably having misinterpreted them. As shown by others, his original interpretation, not his later one, was correct. Judgement is difficult and experiment fallacious.

From a therapeutic point of view, we at present stand in regard to hypophysial disorders about where Kocher and Reverdin stood when they began to operate on patients with goitre to relieve them from dyspnœa and other mechanical effects of the tumour. In the thirty years which have elapsed great strides have been made in our understanding of the disorders of thyroid function, and much of our knowledge has been acquired as the indirect outcome of surgical procedures. It is probable, however, that operations for thyroid disease of one sort or another have reached their peak. We have not only learned much regarding prevention, but even when goitre is established we now know that there are other methods of treatment which prove effective in many cases.

Though the problem is more difficult, it is not at all unlikely that the

surgery of the pituitary adenomata will run a similar course; and, profiting by the experiences of the past with thyroid disorders, we may hope it will be a shorter one. At present, however, about the best we can do is to combat by some operative measure the loss of vision brought about by pressure of the tumefaction upon the chiasm. We know nothing of the underlying causes, so that prevention is beyond our grasp, but we are at present encouraged to believe that certain of the adenomata are amenable to radiation. This, however, as seems to be true of the thyroid adenomata, may prove a disappointment, and that accidents may occur from too vigorous radiation is indicated by the experience in the case which the authors have selected in order to illustrate the condition of gigantism.

It is such a combination of clinical and pathological studies as Mr. Dott and Dr. Bailey have made that is most likely to accelerate not only advances in diagnosis and treatment, but—what is more important—a better understanding of the underlying factors provoking these diseased states.

HARVEY CUSHING.

SUMMARY OF CONTENTS.

I.—INTRODUCTION.
II.—PATHOLOGICAL ANATOMY.
Chromophobe, chromophil, mixed, and malignant adenomata.
III.—THE CLINICAL SYNDROMES. CASE REPORTS.
A. Chromophobe adenomata: (1) With slight constitutional change; (2) Of adolescence with infantilism; (3) In a young adult with hypopituitarism; (4) In middle age with hypopituitarism.
B. Chromophil adenomata: (5) With gigantism; (6) With acromegaly.
C. Mixed adenomata: (7) With mixed syndrome.
IV.—SYMPTOMATOLOGY.
V.—PHYSIOLOGICAL CONSIDERATIONS.
VI.—DIFFERENTIAL DIAGNOSIS.
VII.—TREATMENT.

I. INTRODUCTION.

In papers dealing with the subject of hypophysial lesions it has been customary to merge the many disorders of the pituitary gland in a general discussion of their symptomatology, pathology, and treatment. We do not presume to decry such discussions of past years. They have thrown much light upon a subject which was dark, and which still presents many obscure places, just as did discussions upon 'fever' as a disease entity in former times. However, it is our belief that the knowledge of pituitary disease has now reached a point at which it is advantageous to depart from this custom, and to select a specific lesion of the hypophysis for consideration of its various aspects. To this end we shall deal in this communication with the pituitary lesion of most frequent occurrence—*the hypophysial adenoma.*

It is idle to speculate upon who may have first described one of these adenomata, for in the earlier writings the terminology was so obscure that

many hypophysial tumours were regarded as 'sarcomata'. Indeed, much of the recent literature shows little advance in this respect. To Benda[2] great credit is due. He dispelled much of the obscurity in which neoplasms of the gland were enveloped, by his stress on the fact that histological methods which are adequate to display the normal structural characters of the gland must be employed in the study of its morbid states. In short, for the differentiation of these tumours histological methods must be employed more specific than the customary routine hematoxylin and eosin stains after fixation in Zenker's fluid. By the use of special methods Benda showed conclusively that many of the so-called 'sarcomata' of the hypophysis were composed of specific pituitary cells, and that therefore these tumours were adenomata.

The present communication is based upon the histological study of the 162 hypophysial adenomata in the Brigham Hospital series (to May 1, 1924) and upon a review of the clinical records of the patients from whom the specimens were obtained.* The histological material was secured at operation in all but one instance, and we find ourselves in a position to differentiate certain types of these adenomatous tumours and to link with each of them a distinct clinical syndrome. The relationship between the histological findings and the constitutional aspects of the disorders in question has been practically constant in the entire series of cases.

II. PATHOLOGICAL ANATOMY.

Gross Appearances.—The anterior hypophysis (pars distalis) is structurally akin to other glands of internal secretion, notably the thyroid and adrenal glands, and its adenomata present characters similar to corresponding tumours of these other organs. The hypophysial adenoma is a soft homogeneous mass of epithelial tissue, varying in colour from a white, brain-like appearance to a dark maroon colour. It is usually of a pale yellowish or pinkish tint. Like other adenomata, its rate of growth may outstrip its vascular resources, and it is often subject to local degenerative and hæmorrhagic changes on this account. Consequent upon these processes the formation of cystic cavities is not uncommon. Of the 162 cases in the present series, 28 contained cysts large enough to attract notice during operation.

While the hypophysial adenoma does not differ essentially in its general structure from the same tumour in other organs, its confined position has a striking influence on its behaviour and appearance. A thyroid adenoma as a sharply defined, circumscribed, globular mass can grow to large dimensions without encountering serious resistance. The hypophysial adenoma, on the other hand, encounters resistance from its very inception. With the intrinsic proliferative power of a neoplastic formation it begins to enlarge in its confined cell, bounded by resistant structures—bone and dura mater. The least resistant structure which the tumour meets is its parent gland, the hypophysis, which is largely or completely destroyed by compression. But ere long the

* The cases in Dr. Cushing's Johns Hopkins series, many of which comprised the basis of his monograph (1912)[1], are not included in this study.

dural capsule becomes distended and bulges upward under the chiasm. Even the bony sella itself gives way to the persistent pressure ; it becomes enlarged, ballooned out, and its walls undergo pressure absorption. This is the usual condition in the majority of the cases with the growth still confined within its distended dural and bony encasement.

If left to itself, however, the tumour, still persistently enlarging, now takes the path of least resistance, which varies in individual cases. Commonly the limiting diaphragm of dura above it becomes attenuated and finally gives way, permitting the growth to enter the cranial cavity. This initial intracranial extension is often median, and takes place anterior to or sometimes behind the optic chiasm. In other cases it extends laterally, either free in the intradural space, or the growth may insinuate itself between

FIG. 222.—Coronal section of a brain, showing chromophobe adenoma. Note carotid arteries embedded in tumour.

the dura and the bone of the temporal fossa. On the other hand the upper diaphragm may remain intact, and the growth, through pressure erosion of the sellar floor, may project downward into the sphenoidal cells, where it is found covered by little more than shreds of the dural capsule, a few thin flakes of bone, and the mucous membrane of the cells.

The extensions that these simple adenomata will make under the influence of confinement are at times truly extraordinary, and have often given rise to the erroneous belief that the tumours are of a malignant nature. In one instance such an outgrowth extended between bone and dura across the temporal fossa, eroded the squamous portion of the temporal bone, and appeared outside the cranium beneath the temporal muscle. Not uncommonly in its

lateral extension the growth embeds and surrounds the extradural portion of the internal carotid arteries (*Fig.* 222), and may even extend into Meckel's cave.

Its intradural extensions in advanced cases are no less remarkable. It usually projects upwards as a rounded mass, elevating the optic chiasm, while the optic nerves and tracts are deflected on to its lateral surfaces, and, stretching round it, are compressed and flattened. It sinks its summit deeply into the base of the brain, sometimes compressing the hypothalamic region to the extent of obliterating the third ventricle, at other times indenting the uncinate region on either side. Under the influence of increasing compression and confinement, processes of the tumour may extend into every available crevice: upward, between the brain-stem and temporal lobe; backward, as a thin tongue-like process over the surface of the tentorium or through the hiatus tentorii to the cerebello-pontine angle.

Though these simple adenomata, as will be seen, show unmistakable differences in their finer microscopic structure, to the naked eye they are indistinguishable.

Microscopic Structure.—The pars distalis of the normal hypophysis, it will be recalled, is composed of columns of polygonal cells between which are found small blood-channels supported by a scanty connective-tissue framework. The cells may be divided into two main classes in accordance with their differing affinities for dyes. We thus distinguish the chromophil cells, which have such an affinity, from the chromophobe cells, which do not. The chromophil cells are subdivided by the specific staining affinities shown by the granules contained in their cytoplasm. One type of granules stains with eosin, acid fuchsin, neutral dyes, etc.; they are usually known as the eosinophilic granules. The other type stains with alum hematoxylin, kresofuchsin, acid violet, etc.; and they are commonly designated basophilic granules. The terms acidophilic, versus basophilic, are relics of a time when one type of granules was erroneously supposed to have an affinity for acid dyes and the other for basic dyes. It is preferable, therefore, to use some non-committal designation, and we shall refer to them as *alpha* or *beta* granules (*Fig.* 223, *A*).

Many synonyms exist for these cell types—(1) *Chromophobe* = chief cells, reserve cells, siderophil, etc.; (2) *Chromophil*: (*a*) *Eosinophil* = acidophil, fuchsinophil, oxyphil, etc.; (*b*) *Basophil* = cyanophil, etc.—in accordance with theories of their staining reactions or with varying views regarding their function. From each of them adenomata may take origin. The chromophobe adenoma is by far the most common; the eosinophilic tumour is not infrequent; the basophilic is rare, and is known to exist only as a minute, almost microscopic nodule.

Loewenstein[3], who has made a careful study of the site of origin of hypophysial adenomata, states that they are encountered most frequently in one of three situations in early stages of their development: (1) In the pars intermedia; (2) In the peripheral part of the pars distalis; and (3) In the vicinity of the stalk (pars tuberalis). It is in these parts that the chromophobe cells predominate; and the fact that they are embryologically the least highly differentiated cells of the hypophysis perhaps explains both the

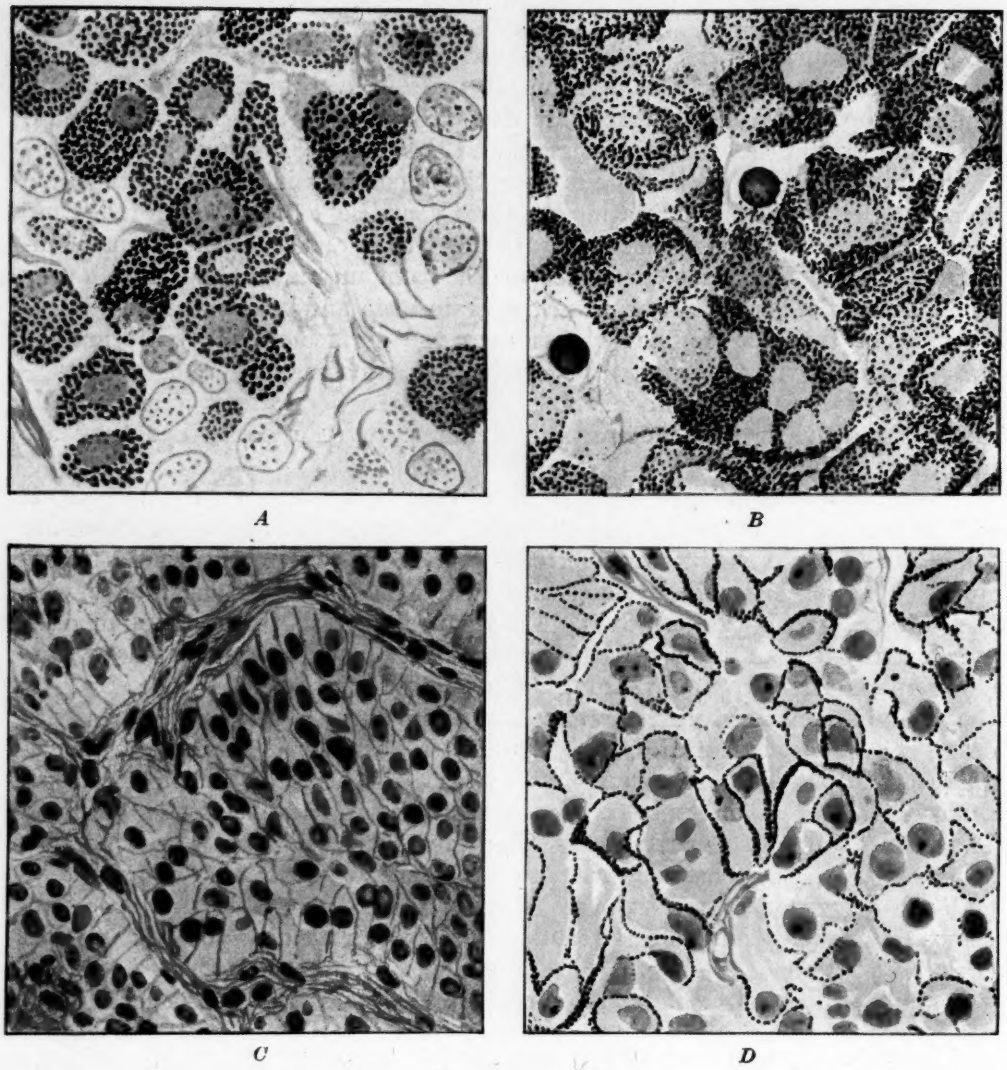


FIG. 223.—*A*. Normal pars distalis. Acid fuchsin-acid violet stain on Regaud-fixed tissue. Alpha granules red; beta granules dark blue; other structures pale blue.

B. Typical adenoma from a case of acromegaly. (P.B.B.H., *Surg. No.* 15505.) Neutral ethyl-violet-orange G stain on Regaud-fixed tissue. Alpha granules violet; other structures orange.

C. Typical chromophobe adenoma from a patient with 'hypopituitary' syndrome. (P.B.B.H., *Surg. No.* 19512.) Hematoxylin and eosin stain on Regaud-fixed tissue. Such an adenoma stained as *A*, *B* or *D* would show no granules whatsoever.

D. Adenoma from a patient with a mixed clinical syndrome. (P.B.B.H., *Surg. No.* 19907.) Neutral ethyl-violet-orange G stain on Regaud-fixed material. Alpha granules violet; nuclei slightly stained; other structures orange.

All drawn under oil immersion lens except *C*, which is magnified 300 diameters.

frequency with which adenomata originate in these places and the predominance of the chromophobe type of tumour.

The Chromophobe Adenoma.—This variety of adenoma is associated with evidences of glandular insufficiency. It is by far the commonest tumour, the series containing 107 examples. On a structural basis two types are perhaps deserving of mention: (1) Those in which the columnar structure of the normal hypophysis is maintained in greater or lesser degree; and (2) Those consisting of a mass of cells without architectural arrangement and containing very little connective-tissue stroma. These latter adenomata have sometimes been called 'strumas'.

In the chromophobe elements of the normal hypophysis, areas may be seen where the cell boundaries are indistinct—the so-called 'Kernhaufen'. It is possible that the adenomata of the second type arise from these areas, but the difference in structure is probably to be accounted for by the varying proliferative activity of individual tumours. The adenomata grow by multiplication of cells of the hypophysial columns, which therefore enlarge. These enlarged cell columns are then invaded by capillaries which provide for their adequate nutrition, and in some cases they thereby become divided off into well-formed secondary columns. Those cells of the chromophobe tumours which rest on connective-tissue septa are usually of an elongated, cylindrical epithelial type (*Fig.* 223, *C*), but elsewhere they are apt to be spindle-shaped or polygonal in form. In some of the soft tumours, on the other hand, which have no connective-tissue septa, the cells may appear circular and almost lymphoid in character.

Clinically, this form of chromophobe tumour is the type that is associated with the 'hypopituitary' syndrome. In the tissues from no case which was clinically free from recognizable acromegalic characteristics have we been able to demonstrate any cells containing α or β granules, with the occasional exception of a rare, isolated cell brought into view after a search through many sections.

The Chromophil Adenoma.—*The Eosinophilic Tumour.*—This adenoma is the form which accompanies the hyperpituitary syndrome. Material from 39 cases is available for study. The tumour in some instances is composed wholly of eosinophilic cells (*Fig.* 223, *B*), no cells free from α granules being demonstrable when proper staining methods are used. In the majority of cases, however, though the adenoma be not *purely* eosinophilic, cells containing eosinophilic granules greatly predominate. But even under these circumstances the non-granular cells do not present appearances identical with the cells of the chromophobe adenoma; they are apt to be larger, to have an abundant coarse cytoplasm, and multinucleated cell forms of either type (granular or non-granular) are frequently seen. As a rule these adenomata are of the 'strumous' variety with scant connective tissue, and they are prone to cystic degeneration. In our experience tumours of this type are constantly associated with the syndrome of overgrowth, i.e., acromegaly or gigantism.

The Basophilic Tumour.—This tumour hardly finds a place in a clinical paper, and we mention it here merely for the sake of completeness. As stated above, it occurs only in the form of minute intraglandular nodules, and, so

far as we know, gives rise to no clinical manifestations. There are no examples in the series.

The Mixed Type of Adenoma.—In 13 cases in the series an adenoma of a mixed type has been encountered. Three varieties may be distinguished: (1) The cells resemble those of the chromophil (eosinophilic) adenoma, but either contain no α granules or a few scattered granules only are discernible; (2) The structure resembles that of the chromophobe adenoma, but each cell shows a ring of α granules in its periphery (*Fig.* 223, *D*); or (3) The chromophobe adenoma type again predominates, but the cells contain granules which stain slightly by the eosinophilic dye. These tumours prove to be associated with syndromes in which clinical evidences of both hyper- and hypopituitarism are present. In other words, a mixed clinical type appears to exist in which the features of these two well-recognized conditions are blended in varying proportions and in which the structure of the adenoma reflects the character of the clinical picture.

The Malignant Adenoma.—Hypophysial adenocarcinomata are rare, and the present series contains only 3 examples. In these three cases the constituent cells have shown no granules. Possibly the chromophobe cells, being less highly specialized forms, are more prone to malignant transformation than are the eosinophilic or basophilic elements.

The tumours are varied in structure. At one part distinct alveolar formations are found, closely resembling those of the thyroid gland, but without basement membrane, and sometimes two or more cell rows in depth. In other parts scattered or closely packed masses of cells occupy irregular spaces in the connective-tissue stroma. Everywhere the variety in size and shape of the cells is striking, and all grades of degenerative change are widespread. Mitoses are frequent. Tumour cells, in irregular colonies, may be observed wedging themselves between strands of fibrous tissue and actively invading it.

These malignant adenomata, like other malignant tumours, possess metastasizing as well as invasive qualities. In the only one of our three cases in which post-mortem information on the point was obtainable, metastases were present in the liver; the hepatic lymph glands were also involved and were probably secondarily invaded from the liver. The metastatic growth presented a structure identical with that of the original hypophysial tumour.

III. THE CLINICAL SYNDROMES.

Apart from the neighbourhood signs and symptoms produced by pressure of the tumour on adjacent anatomical structures, which may result from any hypophysial adenoma regardless of its histological structure, there occur certain striking constitutional changes in the individual. These chiefly affect growth, metabolism, and the deposition of fat, together with changes in other and allied glands, notably in the gonads which lead to alterations in the primary and secondary characters of sex.

These constitutional manifestations of the adenomata are modified by many factors: by the type of the adenoma; by the degree in which the normal glandular function is interfered with; and by the relation of the onset of the

disorder to age. Admittedly, there are some patients even with large adenomata in whom these secondary derangements might pass unnoticed were it not for the existing tumour; and other cases in which apparently identical bodily changes occur without clinically demonstrable tumour. Nevertheless, it is far more common for the hypophysial adenomata to be accompanied by constitutional syndromes sufficiently characteristic to justify their separation into clinical groups. In describing them we shall employ the designations coined by Cushing in 1909,[4] viz., hyperpituitarism, hypopituitarism, and dyspituitarism. By the selection of recent examples which have come under our personal observation in the Clinic, we shall endeavour to illustrate the several types in accordance with the following classification :—

A. Tumour symptoms with slight constitutional disturbance.

B. Outspoken 'hypopituitary' syndrome: (1) Infantile type; (2) Adult adiposo-genital type; (3) Wrinkled atrophic type.

C. Outspoken 'hyperpituitary' syndrome: (1) Gigantism; (2) Acromegaly.

D. Mixed or 'dyspituitary' syndrome.

This terminology is not entirely satisfactory. We do not believe that all the symptoms shown by the patients we have grouped under 'hypopituitary' syndromes are due to suppression of the function of the hypophysis. Moreover, although gigantism—which Krumbhaar terms hyperprepituitarism—is apparently a manifestation of increased activity of the pars distalis, acromegaly is not so certainly due to the same cause, but may, as often stated, be the result of a perverted secretion.

Furthermore, being doubtful whether adiposity is actually due to an hypophysial lesion, and wishing to include the group of non-obese cases to which Cushing for some years has called attention in his clinics, we were unable to use the term dystrophia adiposo-genitalis as synonymous with loss of hypophysial function. We were tempted, therefore, to introduce a new term, 'raripilogenital syndrome' (L. *raripilus*, scanty hair), which would cover both the adiposo-genital and wrinkled atrophic types, emphasizing the symptoms common to both—namely, the cutaneous and genital changes—but we repented in time of our desire further to complicate a subject already overburdened by terminology.

In the main we believe the concepts of hypo- and hyperpituitarism are correct, and with the reservations we have just made we shall continue to use them. The development of these concepts is interesting. They of course had their beginning in 1886, when Marie[5] established the clinical entity which he called acromegaly, and when Minkowski[6] in the following year pointed out the relation of the disorder to the hypophysis. Though Marie first regarded the syndrome as due to hypofunction of the hypophysis, Massalongo[7] considered it to be due to a continuance in post-fœtal life of the function of the hypophysis and thymus. In the same year he pointed out the relationship of gigantism to acromegaly, a view which was further developed in 1895 by Brissaud and Meige.[8] Meanwhile efforts were made by Horsley and others to reproduce these states or their counterpart in the laboratory by pituitary extirpations. These efforts were ineffectual, and naturally enough the idea as expressed by Tamburini[9] in 1894, that acromegaly, at least in its early phase, was an expression of glandular hyperactivity, began to prevail.

During this time pituitary tumours accompanying acromegaly had unfortunately been described under a variety of terms, as sarcomas, gliomas, cylindromas, etc., and it is to Benda's credit that in 1900 he made clear that they were all adenomata of the gland. A year later, from a study of the hypophyses from four cases, he, with Fränkel and Stadelman,[10] came to the conclusion that the hyperplasia of the chromophil cells which was present in all of them probably indicated an increased activity of the gland. The interpretation of this finding as an evidence of hyperfunction was without experimental control—such as Halsted's experimentally produced hypertrophy in the case of the thyroid—and of course was purely a matter of conjecture.

During the next several years confusion was added to the subject by the report of certain cases of pituitary tumours, many of them adenomata, in which no recognizable symptoms of acromegaly occurred. One of the first of these was reported in 1900 by Babinski.[11] He ascribed to a lesion of the hypophysis the genital hypoplasia which he had observed in a young girl; but he does not seem to have grasped the idea that the condition might be due to hypofunction. He noted that his patient was somewhat obese, but did not call especial attention to this fact. Fröhlich[12] a year later, in a report of a single case, emphasized the adiposity, and, though he recorded some hypoplasia of the genitalia, in summarizing his syndrome he mentioned specifically only the adiposity and the cutaneous changes together with the tumour—the presence of which was betrayed by the defect in the visual fields—as the essential features of the condition. Nowhere does he suggest that these symptoms might be due to hypofunction of the hypophysis.

Bartels,[13] in 1906, seems to have been the first to couple adiposity and genital hypoplasia as the essential features of the clinical syndrome which he called 'dystrophia adiposo-genitalis', but stated that a lesion of the hypophysis stood in no causal relationship to the syndrome. About the same time ophthalmologists, gynæcologists, and neurologists (Axenfeld, Miller, Cushing, Kon, and others) had begun to report cases in which adiposity, amenorrhœa, or sexual dystrophy were associated with pituitary tumours.

An explanation of these various and confusing syndromes had to await the experimental reproduction of allied states in the lower animals. It was not even known at this time that the hypophysis was anything more than a vestigial organ as unimportant to the economy as the pineal body or thymus. This view was generally held until 1907, when Paulesco[14] reported a series of operations on the gland by a new method of approach which showed that its complete removal was incompatible with the maintenance of health or perhaps even of life. These experiments were repeated in the following year by Cushing[15] and his collaborators, and they were the first to point out (1909) that a condition resembling adiposo-genital dystrophy was a consequence of partial hypophysectomies in the adult dog.. A year later Aschner[16] showed that skeletal infantilism could be produced by similar operations on puppies. These observations for the first time furnished a dependable proof that lowered function of the hypophysis was the primary factor in the various and imperfectly understood clinical syndromes which had been previously escribed.

Though by the injection of its extracts physiologists had shown the presence of an active principle in the posterior lobe, its removal was unattended by obvious consequences. On the other hand, as noted above, it had long been recognized that definite symptoms followed experimental injury to the anterior lobe—dwarfism, genital hypoplasia, etc., but the negative results of injections of its extracts failed to confirm the association between the anterior lobe and these symptoms. Nevertheless, it was assumed that these symptoms both in the laboratory and clinic were due to hypophysial insufficiency, while as a natural corollary gigantism and acromegaly were associated with glandular over-activity. Though this had been previously conjectured, experimental proof was lacking until the recent studies of Evans and his collaborators[17] demonstrated that actual gigantism may be induced, and the dwarfism, etc., of experimental hypopituitarism relieved, in rats by the intraperitoneal injection of freshly prepared anterior-lobe extracts.

FIG. 224.—*Case* 1. To show the enlarged sella. (× 1.)

CASE REPORTS.

A. CHROMOPHOBE ADENOMATA.

Chromophobe Adenoma with Slight Constitutional Disturbances.—In presenting our illustrative cases, we may well begin with a chromophobe adenoma in its simplest clinical form—namely, a growth large enough to cause well-defined neighbourhood symptoms without provoking any but the most inconspicuous constitutional evidences of disturbed glandular function.

Inasmuch as the patient was a woman who had passed the menopause, there is missing in the clinical picture even the customary sign of symptomatic amenorrhœa.

Case 1.—*Surg. No.* 20950. **Chromophobe adenoma in adult with local symptoms alone. Transphenoidal operation. Considerable improvement in vision.**

ADMISSION.—March 18, 1924. Mrs. F. H., age 49, a housewife of English birth, referred by Dr. W. E. Bruner, of Cleveland, Ohio.

CLINICAL HISTORY.—She has lived an active, normal life with no significant illnesses. Married at 21 years, she has had four normal pregnancies—three healthy children alive and well, and one stillbirth. Her youngest child is 17 years old—i.e., her last pregnancy occurred in her 31st year. Her husband is living and well. She had no wish to avoid a further pregnancy, but none took place. Menstruation began at the age of 14 years and had been quite normal and regular until the age of 47 years (18 months ago), when it abruptly ceased—apparently quite a normal menopause. One year ago vision began to fail and has progressively deteriorated. She has herself observed that the defect involved the temporal fields of vision. Four months ago she began to see double, and her friends remarked that her left eyelid drooped slightly. These conditions persist to the present time.

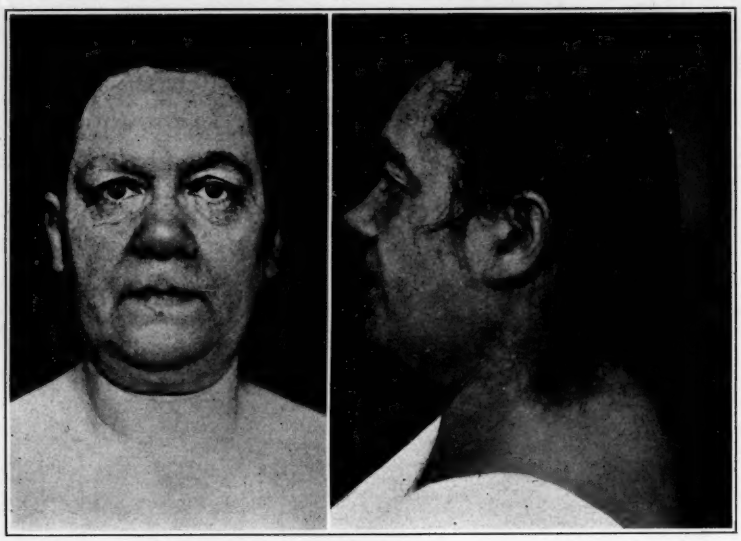


FIG. 225.—*Case* 1. Photographs of patient.

She has always been stout, and during the past twenty years her weight has probably increased slightly, but not more than advancing years would reasonably account for. She has experienced no unusual thirst, nor has she noted any unusual frequency of urination. She has had no headaches.

EXAMINATION.—The following positive neighbourhood findings were revealed: a bilateral primary optic atrophy of moderate degree; V.O.S. 20/30; V.O.D. 30/40; bitemporal hemianopsia—the temporal defect not quite complete on the left side; history of diplopia, but no obvious strabismus. X rays show the sella turcica widely expanded (*Fig.* 224); the floor is irregular in outline and depressed into the sphenoidal sinus; the anterior and posterior clinoid processes are eroded.

She is a stout, vigorous woman of middle age (*Fig.* 225), intelligent and co-operative. Height 159 cm., weight 86·2 kilo. The skin is of normal texture, humidity, and colour. The hair is entirely normal in quality, quantity, and distribution. The basal metabolic rate is − 9 per cent. There is a slight, moderate, diffuse enlargement

of the thyroid gland, of frequent occurrence in the Lake district, where she lives. She presents no symptoms suggesting thyroid dysfunction. One X-ray treatment was given while she was awaiting her operation, with no subsequent appreciable change in the visual fields.

Operation.—March 28, 1924. Dr. Cushing exposed the bulging sellar floor by the usual sublabial and transphenoidal procedure which he has described. A sellar decompression was performed, and on incising the tense dural capsule of the tumour soft adenomatous tissue was extruded, and a considerable amount of this tissue was removed with a spoon from within the capsule.

Post-operative Course.—She made a rapid and satisfactory recovery from the anæsthetic. Subjective improvement in vision was noted within a few hours. Convalescence was uneventful. At the time of her discharge on April 11 her visual acuity was practically normal. A clear-cut right temporal hemianopsia remained. A second X-ray treatment was given twelve days after operation, and arrangements were made for six further treatments to be given at intervals of three weeks.

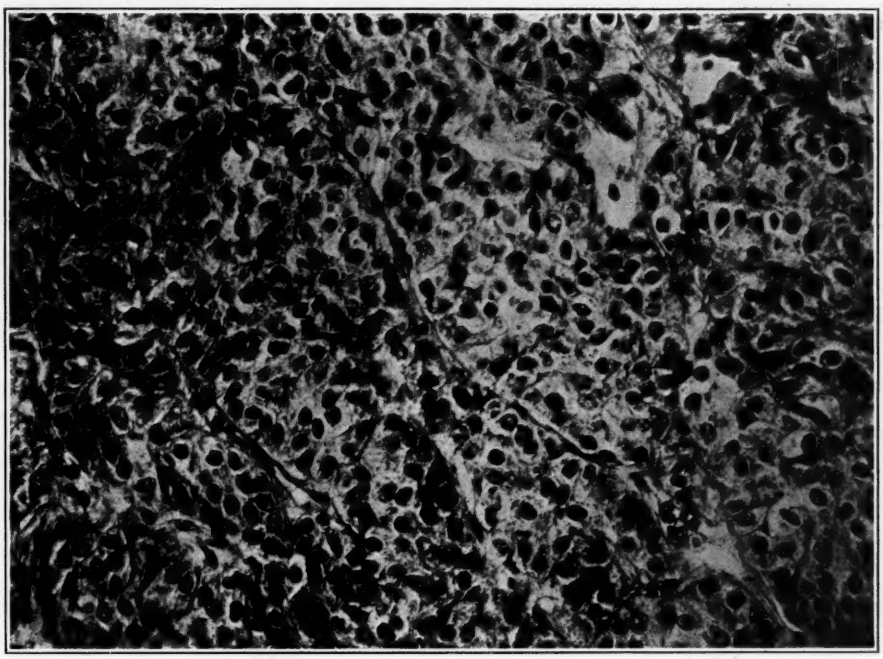


Fig. 226.—*Case* 1. Photomicrograph of chromophobe adenoma. (Hæmatoxylin and eosin stain.) (×300.)

A report of May 9, 1924, from Dr. Bruner, states that " the defect in the temporal field in the left eye is entirely gone, and in the right—which had almost a complete temporal hemianopsia—there is now only slight peripheral contraction—certainly a most gratifying change ".

Pathology.—Sections of the tissue show the tumour to be composed of epithelial cells, arranged in columns from 2 to 6 cells in thickness, very much after the manner of the normal pars distalis (*Fig.* 226). These columns are separated by capillaries with thin walls. The cells have oval nuclei, and in their cytoplasm no granules are to be found except mitochondria.

Diagnosis.—Chromophobe adenoma.

This, then, is an example of a chromophobe adenoma with unmistakable signs of its presence but with practically no constitutional indications of

hypopituitarism. It is true that she was somewhat obese, but this condition had been present for many years without particular change at the onset of her disease. It may be objected that the amenorrhœa should be interpreted as a consequence of the adenoma. In any other disease, however, the menopause occurring at the age of 47 would not excite comment. It is our impression that the pathological amenorrhœa of pituitary insufficiency is of gradual onset, and the abrupt cessation of the menses in this patient leads us to believe it was unconnected with the hypophysial disorder which shortly followed it.

It is evident from the records that a large number of pituitary adenomata in women become manifest either shortly after pregnancy or the menopause; and we incline to the view that the physiological disturbance which these events are known to induce may act as a predisposing factor to adenomatous development in the hypophysis.

Chromophobe Adenoma with 'Hypopituitary' Syndrome.—This, as already stated, is by far the commonest type of pituitary disorder. Of the 162 cases, 107 fall definitely into this category. In each instance a chromophobe tumour was identified. The disease is essentially one of adult life. In the series only 3 cases were recorded in the second decade, the youngest being 14 years old. The numbers were fairly evenly distributed in the third, fourth, and fifth decades of life, and the great majority were credited to them. A considerable number, however, occurred with diminishing frequency beyond the age of 50 years. These figures represent the age of the patient on admission to the hospital; as the average duration of symptoms prior to admission was between three and four years, an adequate idea of the usual age at the onset of the malady may be gained. The sexes are apparently equally afflicted, there being 54 males and 53 females in the series.

The local manifestations of the tumour are the same for all ages, but its secondary or hypopituitary effects are modified considerably by the age of the individual. We give three examples of the disorder: as it appears in the young adolescent, in the young adult, and in the middle-aged patient. As stated, the disease is rare in the extremes of life, and the following case, which has come under our personal observation, is one of the three below 20 years of age. Though the secondary sex characters were well established, the glandular insufficiency occurred early enough to check skeletal growth.

Case 2.—*Surg. No.* 18904. **Chromophobe adenoma of adolescence with partial infantilism. Mistaken for cyst of Rathke's pouch. Transfrontal operation. Considerable improvement in vision.**

ADMISSION.—May 26, 1923. E. H. D., male, age 18, a student, referred by Dr. J. G. Janney, Dodge City, Kansas, with the complaint of failing vision and headaches.

CLINICAL HISTORY.—Though always a very quiet boy and disinclined for rough sports, he had developed quite normally, both physically and mentally, until the age of 15 years, when he practically ceased to grow, and his height has remained at about five feet. At the same time (that is, three years ago) he began to suffer from severe, 'bursting' headaches, which have increased progressively in severity and frequency. They have recently been accompanied by vomiting and followed by a marked degree of somnolence, lasting on occasions for twenty-four to thirty-six hours. Three years ago also, his vision began to fail; it has become gradually worse, and he has been aware of bitemporal blindness.

As a child, he had a good soprano voice, but at 15 it 'broke'; it, however, did not attain the normal male bass, but remains irregular and high in pitch. A year later, after what appears to have been a normal adolescence, his youthful libido was lost, and he observed that nocturnal emissions no longer occurred. He began to experience increasing difficulty in concentrating on his studies. During the past eighteen months he has noted increased thirst, has had to urinate more frequently during the day, and has had to rise at least once during the night on this account. Until a year ago he had been a very slim boy, and for some time previously his weight had remained about 38 kilo. During the past year he has gained 11·3 kilo. in weight. He has had occasional slight epistaxis, and his eyes have become more prominent in the past year.

FIG. 227.—*Case* 2. To show the ballooned sella. (× 1.)

EXAMINATION.—The following positive findings were revealed: *Local.*—A bilateral primary optic atrophy, with bitemporal hemianopsia; V.O.S. 20/100; V.O.D. 20/50. The X-ray disclosed a widely distended sella its floor slightly depressed, and the posterior clinoid processes and dorsum sellæ extensively eroded (*Fig.* 227). Moderate bilateral exopthalmos.

General.—Owing to his short stature, slight skeletal frame, and moderate adiposity, he presents the appearance of a boy of fourteen (*Fig.* 228). Height slightly over 5 ft. (156·2 cm.); weight 49 kilo. He is quite beardless. The hair of the scalp, though abundant, is very soft, silky, and fine. The axillary hair is very scanty; on the pubes it is sparse and has a distribution of feminine type; the trunk and limbs are hairless. The skin is thin, dry, and pale, and of a fine, soft texture. He is not especially obese, but one notes the characteristic fullness of the breasts, hips, and

lower abdomen. The genitalia are normally developed. A slight degree of genu valgum is present. The basal metabolic rate is – 8 per cent. Observation in hospital shows that his fluid intake and his urinary output are slightly in excess of normal limits—up to 2600 c.c. daily.

A slight opacity just above the greatly enlarged sella could be made out on stereoscopic films, and a presumptive diagnosis was made of an intrasellar tumour of craniopharyngeal pouch origin—a more likely diagnosis than adenoma considering the youth of the patient. Consequently, Dr. Cushing decided to operate by the transfrontal route.

OPERATION.—June 9, 1923. A right osteoplastic flap was reflected, the dura raised from the orbital roof, incised along the sphenoidal ridge, and the frontal lobe, protected by its dura, was elevated to expose the optic nerves and chiasm. A reddish mass elevating the chiasm and projecting upwards between the optic nerves was disclosed, obviously an adenoma. The dural capsule was incised and a sufficient portion of the tumour was removed to free the chiasm and optic nerves from pressure. The bone flap was replaced and the wound closed in layers as usual.

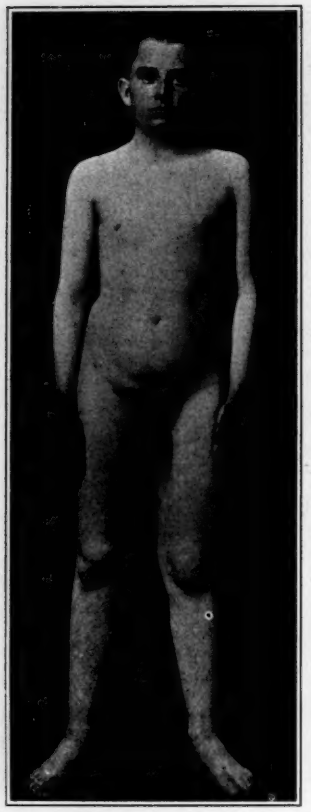


FIG. 228.—*Case* 2. Photograph of patient, age 18; height 5 ft.

Post-operative Course.—Recovery from the operation was uneventful, though there was a temporary increase in the polyuria, which amounted to 5000 c.c. on the fourth day, but gradually subsided to the pre-operative level. Vision improved remarkably, the acuity rising to V.O.S. 20/50, V.O.D. 20/20, and the fields expanding to normal limits within three weeks. Headache, vomiting, and somnolence were entirely relieved. One X-ray treatment was given fourteen days after the operation.

Reports from the patient and his physician subsequent to his discharge relate that he remained well and at work as an office boy until some five months later, when he again began to suffer from headaches, and at the same time his polyuria increased once more to between 3000 and 4000 c.c. daily. He was given two X-ray treatments with prompt and complete relief.

PATHOLOGY.—The tissues removed show (*Fig.* 229) the tumour to be composed of elongated epithelial cells, divided into definite cell columns by blood sinuses. The connective tissue is confined to the thin walls of these sinuses. The epithelial cells form in places a pseudostratified epithelium with the bases of the cells on the blood sinuses. The cytoplasm of the cells is vacuolated extensively, and no granules are to be found except mitochondria.

DIAGNOSIS.—Chromophobe adenoma.

This is the nearest approach to a case of infantilism in the series of hypophysial adenomata.* Infantilism, when occurring in association with a hypophysial tumour, is so constantly related to a congenital tumour (tumour of Rathke's pouch) that in this case, although positive evidence of

* Since this review of the clinical histories by Mr. Dott, there has been in the Clinic an example of typical chromophobe adenoma with ballooned sella in a child of 10 years with skeletal infantilism and adiposity, much more commonly associated with craniopharyngeal pouch tumours.—P. B.

a suprasellar lesion was lacking, a transfrontal operation was performed, whereas the operation of choice for hypophysial adenomata with large ballooned sellae is by the transphenoidal route from below. The significance of polyuria will be discussed later; it is to be regarded as incidental, and not as a peculiar characteristic of this type of pituitary disease.

The following is a typical example of the disease in a young adult in whom there were constitutional evidences of glandular insufficiency of the adiposo-genital type. The case differs in no essential respects from some hundred others which fall in the central age group.

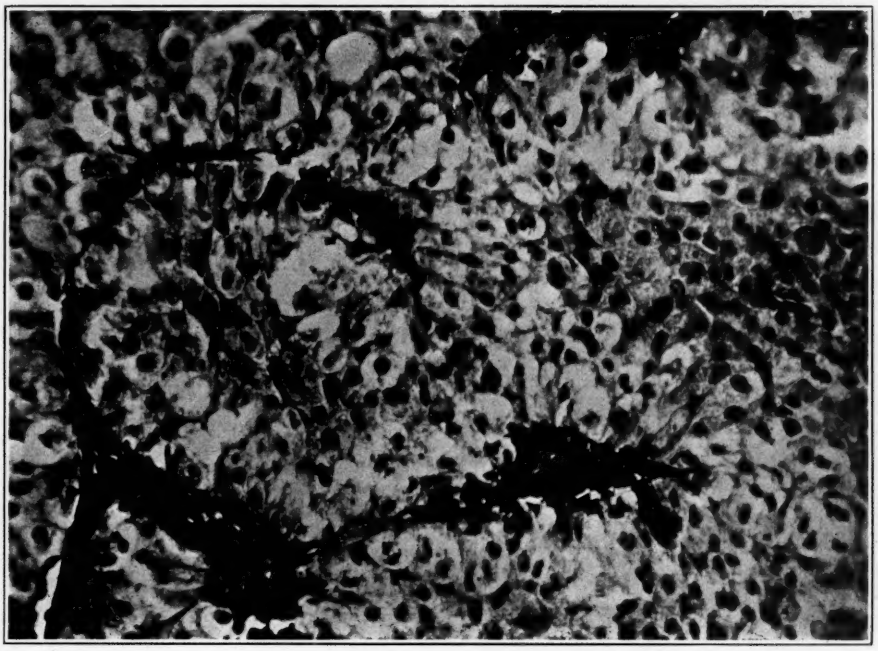


FIG. 229.—*Case* 2. Photomicrograph of chromophobe adenoma. (Hæmatoxylin and eosin stain.) (× 300.)

Case 3.—*Surg. No.* 20323. **Chromophobe adenoma with hypopituitarism in a young adult. Operation, with improvement in vision.**

ADMISSION.—Dec. 14, 1923. Benjamin F., age 27 years, unmarried, a Jewish house painter, referred by Dr. J. R. Shannon, of New York City, with the complaint of failing vision and of headaches.

CLINICAL HISTORY.—He has always been rather obese, even as a boy; his parents and brothers and sisters are also rather stout—one sister remarkably so. During the past year he has not gained, but has probably lost slightly in weight. Fourteen months ago he awoke one morning to find that his vision had suddenly failed to an alarming degree. He was unable to read and noted that his lateral fields of vision were gone. Not long thereafter he observed that sexual libido, which had never been very active, was in total abeyance, and that his normal nocturnal emissions had ceased. Ten months ago he began to suffer from headaches, at first mild and generalized, but progressively increasing in severity, and recently referred to the back of the eyes. He has complained of loss of interest and ambition in his work, and of becoming easily tired.

FIG. 230.—*Case* 3. To show outline of sella. (× 1.)

FIG. 231.—*Case* 3. Photographs of patient of adipose type.

EXAMINATION.—The following objective findings were revealed: *Local.*—Bilateral primary optic atrophy; V.O.S. 20/50; V.O.D. light perception only; bitemporal hemianopsia. X rays show the sella turcica greatly expanded, its floor depressed into the sphenoidal sinus, and its anterior and posterior clinoid processes eroded (*Fig.* 230).

General.—There is a moderate degree of somnolence; he is somewhat dull, heavy, stupid, and grossly obese (*Fig.* 231). There are heavy deposits of subcutaneous fat over the shoulders, lower part of abdomen, and hips. Height 165 cm., weight 111 kilo. The skin is fine and soft in texture. The hair of the scalp is sparse, fine, and silky. The beard is very scanty, as is the hair of the axillæ. The pubic hair has a definite, sharp, upper limit of feminine type. The genitalia appear normal. The temperature tends to be slightly subnormal. The pulse is slow, varying between 60 and 70 per minute. The basal metabolic rate is — 8 per cent.

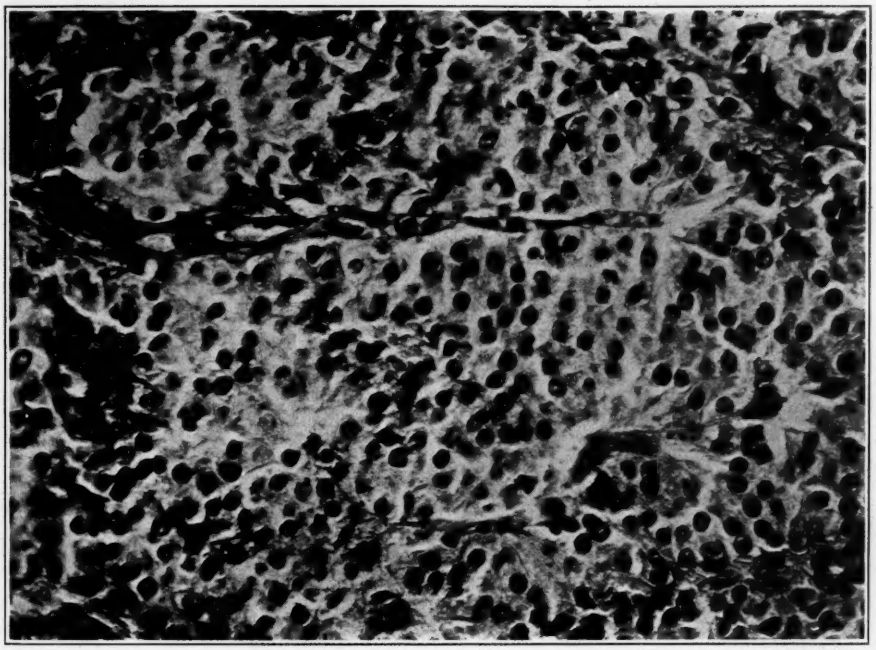


FIG. 232.—*Case* 3. Photomicrograph of chromophobe adenoma. (Hæmatoxylin and eosin stain.) (× 300.)

OPERATION.—Dec. 26. Dr. Cushing exposed the bulging sellar floor by the usual transphenoidal route. The tumour had already burst its dural capsule and, covered by mucous membrane alone, was protruding into the sphenoidal sinus. This portion of the growth, together with the remaining fragments of the sellar floor and some of the intrasellar growth, was removed.

Post-operative Course.—There was a rapid and uneventful recovery. Definite improvement of visual acuity and a slight expansion of the visual fields were evident on Jan. 13, 1924, when he was discharged. One X-ray treatment was given fourteen days after the operation, and radiation at intervals of three weeks was advised. He reported on July 22, 1924, that he was feeling well and vision was slowly improving.

PATHOLOGY.—Sections show the tumour (*Fig.* 232) to be composed of elongated epithelial cells, with small oval nuclei. The cells are divided roughly into thick cell columns by small capillaries and occasional larger thin-walled blood sinuses. The connective tissue is practically confined to the walls of the blood-vessels. The cytoplasm of the cells contains no granules except mitochondria.

DIAGNOSIS.—Chromophobe adenoma.

The outstanding features of this very typical example of a pituitary tumour in a young adult are: (1) The neighbourhood symptoms of the growth, and particularly the loss of vision, which led to his admission to a surgical ward; (2) The constitutional signs of adiposity, hypotrichosis, somnolence, lowered basal metabolism, and so on. As anticipated, a chromophobe adenoma was disclosed.

The following case portrays the disease as it is frequently encountered in the middle-aged and elderly, who show what in this Clinic has long been designated as the wrinkled (and often lean) type of pituitary insufficiency.

Case 4.—*Surg. No.* 19512. **Chromophobe adenoma of middle age with hypopituitarism. Operation. Improvement in vision.**

Admission.—Aug. 23, 1923. Mr. J. A. K., age 52, married, a bookkeeper of English birth, referred by Dr. D. H. Bell, of Tacoma, Washington, complaining of failing vision.

Fig. 233.—*Case* 4. To show the enlarged sella. (× 1.)

Clinical History.—After a normal childhood he showed during youth a disinclination for rough outdoor sports. He has never had to shave more than two or three times in a month. He married; two children were born to him; the elder, a boy, was killed in the war; the younger, age 17, is a healthy girl. His wife is living and well. Two years ago he began to lose initiative and ambition in his work, and has become progressively more listless and apathetic. During this time he lost his potentia sexualis. Eighteen months ago his eyesight began to fail. His lateral fields of vision were subjectively the first to be lost. His left eye has been blind for the past two months, and vision for reading has been lost on the right. He

has had no headache, nor has he experienced unusual thirst or excessive frequency of urination. His weight has not altered appreciably during the past thirty years.

EXAMINATION.—The following positive findings were revealed: *Local.*—An advanced bilateral optic atrophy; V.O.S. light perception only; V.O.D. 5/200. Though he gives a clear history of bitemporal hemianopsia, the vision of the left eye is at present too poor to estimate its field; a right temporal hemianopsia is present. X rays show the sella to be distended, its floor depressed into the sphenoidal sinus, and its posterior clinoid processes absorbed (*Fig.* 233).

General Features.—He is a man of rather spare build; height 168 cm.; weight 64·4 kilo. Complexion is sallow; his skin is thin, soft in texture, very dry, and covered by fine wrinkles (*Fig.* 234), giving the impression of being withered and atrophic. On the scalp the hair is sparse, fine, and dry; it is very scanty on the face and pubes and in the axillæ; it is almost absent from the trunk and extremities.

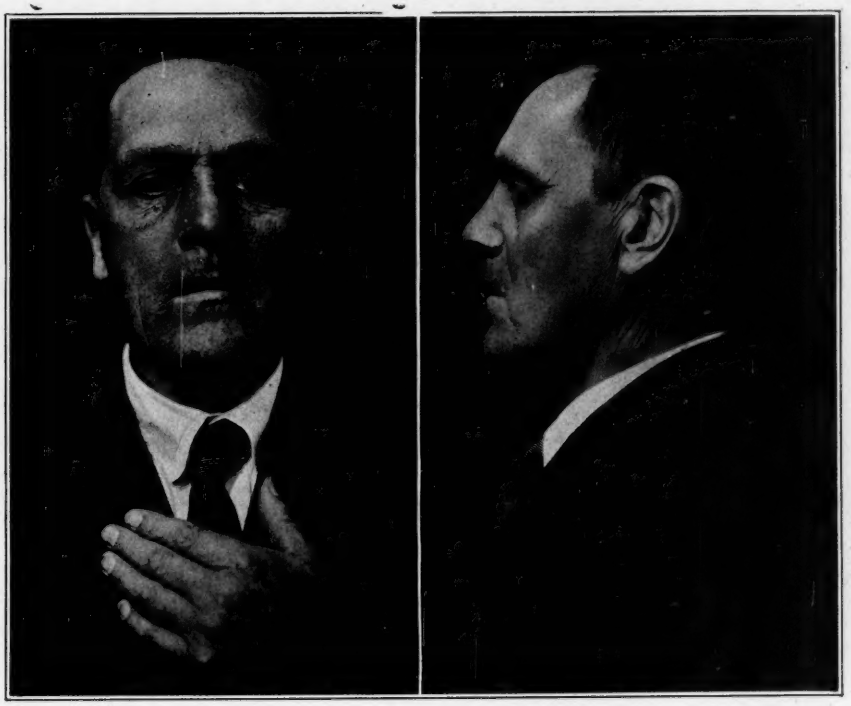


FIG. 234.—*Case* 4. Photographs of patient with wrinkled type of skin.

The genitalia are small but normally developed. The basal metabolic rate is − 4 per cent. His fluid intake and output were normal under observation in the hospital.

OPERATION. — Aug. 30. Dr. Cushing operated, employing the customary transphenoidal procedure. The thin bony floor of the sella was removed and the dural capsule of the tumour was incised. Soft, adenomatous tissue under tension extruded itself through the incision. A portion of the growth was removed.

Post-operative Course.—Recovery was rapid and satisfactory, though with less prompt improvement in vision than usual. He was given a single X-ray treatment, and before his discharge on Sept. 19 some vision had returned to the left eye, to the extent of 5/100, while the acuity of the right had risen to 5/70. The perimeter showed at this time a complete bitemporal hemianopsia. In December he reported himself to be in good condition, and stated that a further improvement in vision had occurred, so that he was able to read the secondary headlines of the papers. He held this gain for nearly a year, when, according to reports, his vision again failed.

PATHOLOGY.—The tissue shows (*Fig.* 235) the tumour to be composed of elongated epithelial cells, divided roughly into thick cell columns by thin-walled blood sinuses. Connective tissue is scanty and confined to the walls of the blood-vessels. The cells have oval small nuclei and fairly heavy cytoplasm in which mitochondria are present but no other granules.

DIAGNOSIS.—Chromophobe adenoma.

The constitutional expression of the disease presented in this man differs from the usual manifestations chiefly in respect of the atrophic changes in the skin and hair, giving the patient a rather shrivelled look. This appearance, less characteristic of the hypopituitary syndrome than is marked adiposity,

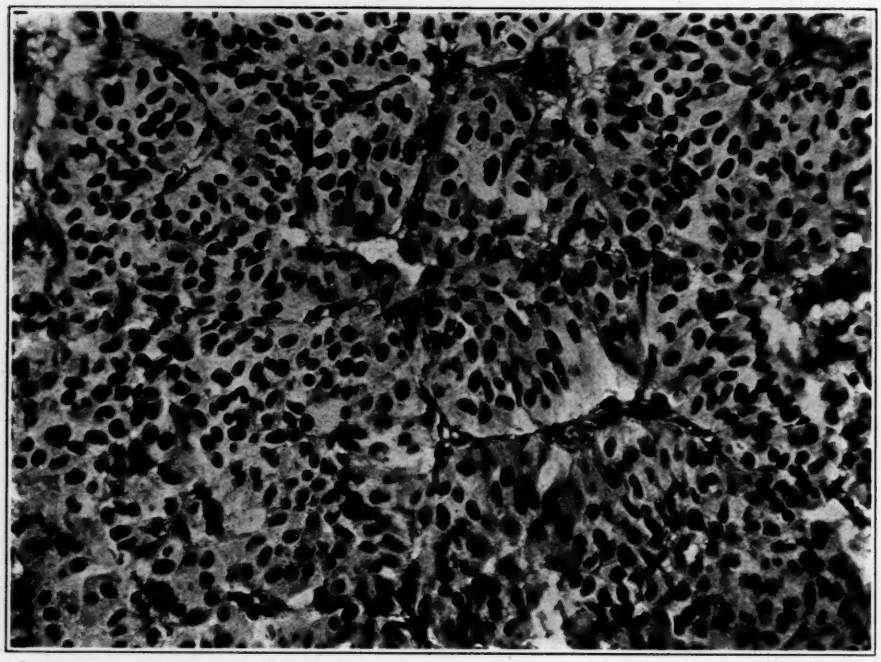


FIG. 235.—*Case* 4. Photomicrograph of chromophobe adenoma. (Hæmatoxylin and eosin stain.) (× 300.)

is nevertheless not uncommon in patients past the prime of life. It may even be seen in young adults, to whom it gives a distinctly under-nourished if not emaciated appearance.

B. CHROMOPHIL ADENOMATA.

Eosinophilic Adenoma with 'Hyperpituitary' Syndrome.—Of the 162 cases, 39 were clinically acromegalic,[19] and in all but 4 an eosinophilic adenoma was identified. The tissues from the remaining four had been improperly fixed, but were in all likelihood of similar structure. The disease is essentially one of adult life. No case below the age of 20 entered the hospital. The numbers are evenly distributed in the third, fourth, and fifth decades of life. Only three cases were beyond the age of 50 at the time of admission. The disease appears to take a more chronic course than that

associated with a chromophobe adenoma. It is well known that the adenoma in many instances of acromegaly presents no surgical problem. The tumour may remain small and the patient may show no neighbourhood symptoms whatsoever. Indeed, widely ballooned sellae are less commonly seen in acromegaly than in hypopituitarism.

The average duration of recognizable acromegalic symptoms prior to admission has been six or seven years. The age incidence of onset is therefore considerably lower than the above figures indicate—a large proportion of cases beginning in the third decade of life, and a considerable number in the second decade. Gigantism, indicating that the disease had begun while growth was still in progress, was present in only four cases. The sexes are affected in approximately equal proportions, the males numbering 18 and the females 21. Below we present two examples of the well-known syndrome : (1) As it affects the adolescent ; and (2) As it occurs in the young adult.

Case 5.—*Surg. No.* 19847. **An eosinophilic adenoma with gigantism. Radiotherapy, with untoward symptoms. Transphenoidal operation. Marked improvement in vision and general health.**

Fig. 236.—*Case* 5. Showing enlarged sella in a case of gigantism. (× 1.)

Admission.—Oct. 8, 1923. Mr. C. V. C., age 21, unmarried, referred by Dr. G. W. Crile, of Cleveland, Ohio, complaining of failure of vision, headache, and weakness.

Clinical History.—Early childhood was uneventful, except for the fact that at the age of 11 years he was struck on the right eye by a tennis ball—an event which

has left some permanent impairment of vision. About the age of 13 years he began to grow rapidly, and soon he towered above his schoolmates. He was not good at games, and, despite his unusual size, when compared to his fellows he was feeble and weak. It soon became apparent that his hands and feet were enlarging to a size out of proportion even to his great stature. He required shoes especially made to fit him.

Three years ago (in his eighteenth year) he had a temporary loss of vision in the temporal field of the left eye. This lasted about one month and then passed off spontaneously. For the past year he has suffered occasionally from mild frontal headaches. He has felt 'nervous' and easily tired. He noted that his hands and feet perspired excessively, and that his limbs were apt to become numb and to tingle if left for long in one position. Lack of ambition, feebleness, and lethargy have been progressive. He has attained the height of 6 ft. 8 in., but thinks he has ceased to grow within the past year. He has noted no unusual thirst nor undue frequency of urination.

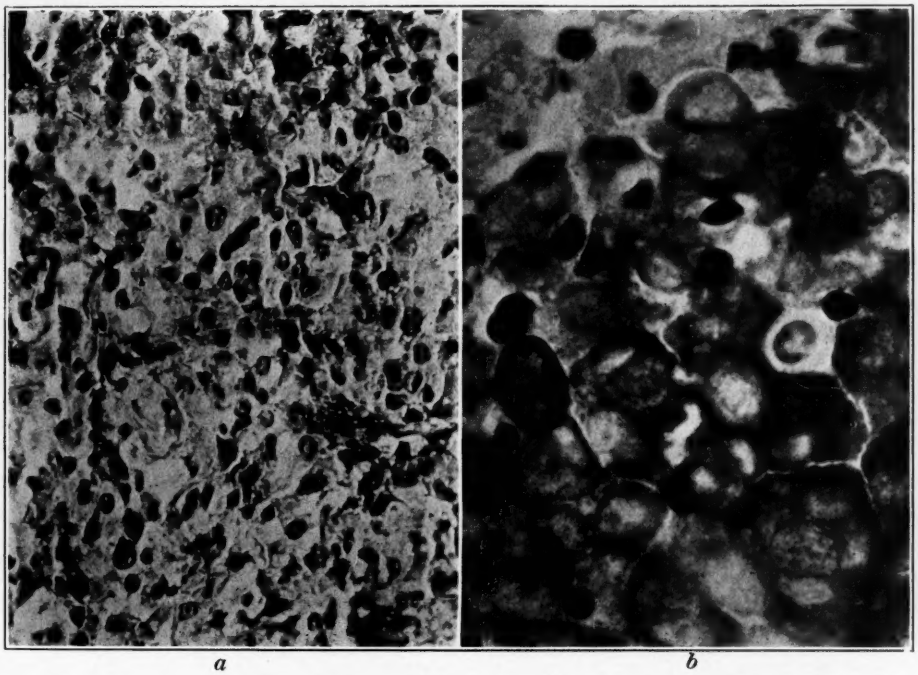
FIG. 237.—*Case* 5. Photographs of patient.

EXAMINATION.—The following positive findings were revealed: *Local.*—There are some patches of old retinitis in the right fundus evidently due to his old injury otherwise the discs appear normal; V.O.S. 20/15; V.O.D. 20/30; visual fields normal, with the exception of two small paracentral scotomata in right field. The X-ray shows a widely distended sella (*Fig.* 236), its floor depressed into the sphenoidal sinus, and both anterior and posterior clinoid processes eroded.

General.—He is a veritable giant (*Fig.* 237), 201 cm. in height and weighing 108·7 kilo. He is heavily built with broad shoulders and expansive chest. Examining the skeletal architecture one notes the prominence of the supra-orbital ridges and the disproportionate enlargement of the facial bones compared with those of the cranium. X rays show a thickened cranial vault and very large maxillary, frontal, and mastoid air sinuses. The jaw is massive, but there is no mal-occlusion of the teeth. There is a moderate degree of pathological kyphosis of the upper dorsal spine. The bones of the limbs are enormous, heavy in build, and their prominences are exaggerated—features which are especially marked in the distal limb

segments. There is moderate hyperplasia of the subcutaneous connective tissues of the hands and feet, giving the fingers a rounded appearance, with well-marked pads on the palmar surfaces. The thickening in the fingers and dorsum of the hand is curiously soft and inelastic. The feet show similar changes. The cutaneous surface itself is not remarkable. The hair is not unusual in quality, quantity, or distribution, with the exception that the beard is scanty for his age. There is profuse sweating of the palms of the hands and soles of the feet. The basal metabolic rate is +5 per cent. He is asthenic, but not drowsy. Libido sexualis has never been very strongly experienced. The genitalia appear normal. The fluid intake and output were normal during observation in the hospital.

In the absence of any definite impairment of vision from pressure involvement of the chiasm, radiation was advised. One X-ray treatment was given in hospital, and arrangements were made for them to be continued at intervals of three weeks at his home. He was discharged on Oct. 17.



a *b*

FIG. 238.—*Case* 5. Photomicrographs of chromophile adenoma. *a*. Hæmatoxylin and eosin stain. (× 300.) After X-ray treatment. Note absence of connective-tissue septa. *b*. Neutral ethyl-violet-orange G stain. (× 850.) Only eosinophilic granules and red blood-corpuscles appear black in photograph.

His general condition improved considerably during the next two months; his headaches were relieved and he felt stronger. However, on Dec. 18, a few hours after his fourth radiation (a prolonged treatment), he had a severe generalized headache, and felt sick and nauseated. He soon noted that his sight was failing and that the lateral field of vision of his left (the good) eye was gone, so that he could see only straight in front of him. He became seriously ill with prostrating headaches and an extraordinary degree of muscular enfeeblement, and on Jan. 11, 1924, was brought back to the hospital.

EXAMINATION.—At this time examination showed a distinct pallor of the left disc, with temporal hemianopsia; V.O.S. 3/200; V.O.D. 20/30. The basal metabolic rate proved to be unaltered, remaining at + 5 per cent. The X rays showed no further change in the sellar outlines.

He was kept under observation in the belief that his exacerbation of symptoms was due to some acute degenerative process caused by the radiation and in the hope that his symptoms would spontaneously subside. However, the left eye gradually became almost blind and the acuity of the right fell to 20/50. His headaches meanwhile remained most severe. Surgical intervention was considered imperative to save vision.

OPERATION.—Feb. 2. Dr. Cushing by the usual transphenoidal approach exposed the 'paper-thin' sellar floor, and a generous decompression was effected, exposing the tense dura over the tumour. On incising the membrane a soft and almost liquid tissue began to exude. The adenoma was largely necrotic in its central part and much of it was scooped away.

Post-operative Course.—In spite of the fact that there was prompt relief from headaches and that within seven days his vision had greatly cleared and sight was returning in the left temporal field, it was long before his general condition of enfeeblement began to improve. Not until three weeks had passed did he regain sufficient vigour to be up and about. During his convalescence he had a remarkable period of polyphagia, being hardly satisfied with five meals a day. By the time of his discharge, Feb. 27, the vision had improved to V.O.S. 20/30, V.O.D. 20/30, and the left temporal field had opened out almost to its normal peripheries.

Subsequent Course.—Later reports state that he made an excellent recovery with unimpaired vision, that he has been free from headaches, and shows much more vigour than for some years past. His last letter, Feb. 2, 1925, tells of his leading an active life on a ranch in the West.

PATHOLOGY.—Sections of the tissue removed at operation show a mass of rounded cells of various sizes without architectural arrangement. Occasionally a thick-walled blood-vessel is seen. There are many multinucleated cells. The cytoplasm of the cells contains numerous fine granules which show a tendency to congregate in the periphery of the cells (*Fig.* 238).

DIAGNOSIS.—Chromophile adenoma.

The essential features of this unusual case are: excessive and disproportionate growth of the skeleton and somatic parts, hyperostoses, slight hyperplasia of the connective tissues, asthenia, depression of sexual function, hyperhydrosis, and so on, in connection with a large eosinophilic adenoma which had given no serious local symptoms until after excessive radiation. The circumstance that the disease afflicted this patient in adolescence makes the clinical picture predominantly that of gigantism. Particular attention may be drawn to the sudden increase of local symptoms following radiotherapy and their relief by operation.

For comparison with the preceding case, the following example of acromegaly has been selected, as the two patients were nearly of the same age on admission. In the acromegalic, however, the disease presumably began after growth had ceased.

Case 6.—*Surg. No.* 20999. **Eosinophilic adenoma with early acromegaly. Transphenoidal operation. Radiotherapy. Recovery without improvement in vision, but apparent abeyance of the disease.**

ADMISSION.—March 24, 1924. Joseph S., age 20 years, unmarried, a machinist, referred by Dr. W. D. Ayer, of Syracuse, New York, with the complaint of failing vision.

CLINICAL HISTORY.—He had developed quite normally until the age of 19 years. At that time he was a well-built, athletic youth, and had done well in school and at his work as machinist. Seven months ago he noted that his shoes—size 8, which size he had worn for some years—had become too tight for him. He observed also that a finger ring he was accustomed to wear had become too small and he was obliged to have it enlarged. His hands became so thickened and increased in

FIG. 239.—*Case* 6. Showing enlarged sella of acromegaly. (× 1.)

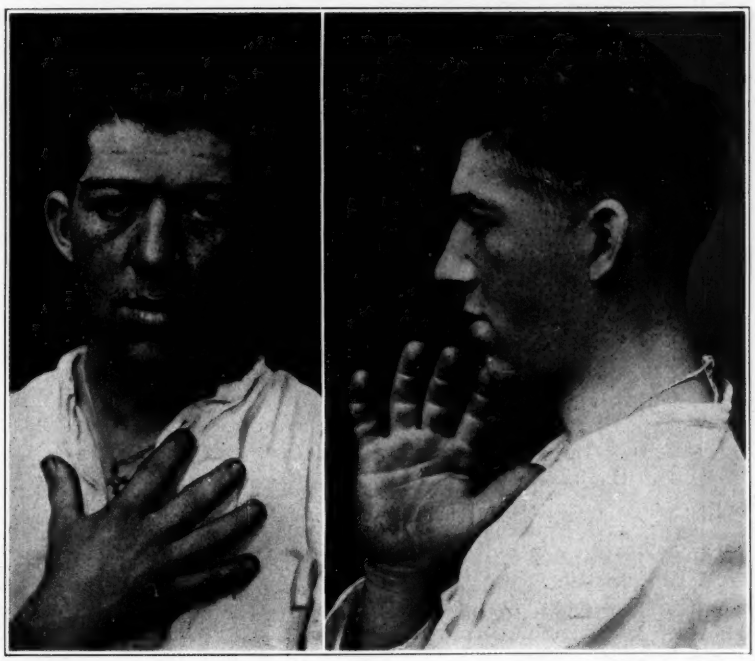


FIG. 240.—*Case* 6. Photograph of young man with early acromegaly.

breadth that he was unable to get on his customary gloves. His friends soon remarked upon a change in his features, especially on the enlargement and thickening of the nose and lips. At about this same time his weight, which had remained fairly constant for several years, suddenly began to increase, and he has since gained 18·1 kilo. Coincidently, his sexual libido disappeared and nocturnal emissions ceased.

Five months ago he had slight epistaxis, which recurred several times a week for about a month. Not long after this his vision began to fail (bitemporally) and has progressively grown worse. At the same time he began to suffer from recurring frontal headaches. These, however, have never been severe.

Four months ago he began to have frequency of urination during the day. At this time his doctor detected sugar in his urine, made a diagnosis of diabetes, and instituted diabetic treatment, which was maintained for about six weeks. His polyuria gradually subsided. Two months later, when all dietary precautions had been discontinued, no sugar could be detected in his urine. (As he had changed his doctor, exact information as to the course of his glycosuria is not obtainable.) He has noted occasional transient diplopia during the past two months. Within the past six weeks he has experienced on three or four occasions the sensation of a peculiar and disagreeable odour, which others could not detect.

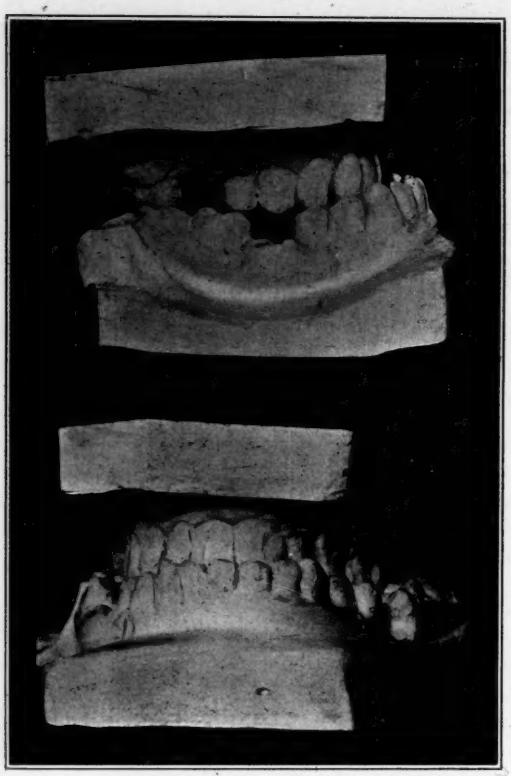


FIG. 241.—*Case* 6. Cast of teeth to show prognathism and mal-occlusion.

EXAMINATION.—The following findings were revealed: *Local.*—Optic discs slightly hazy with veins moderately engorged; no definite pallor; V.O.S. light perception only; V.O.D. 20/200; a temporal hemianopsia is present on the right. X rays show the sella to be widely distended, though not markedly depressed into the sphenoidal cell (*Fig.* 239).

General.—A well-nourished young man (*Fig.* 240) who shows a marked tendency to somnolence, apathy, and disinterest. His height is 174·5 cm. His weight is 71·0 kilo. On examining the skeleton, one notes a marked prominence of the supra-orbital ridges, and the X rays show the frontal and maxillary sinuses to be unusually large; the lower jaw is much too wide for the upper, so that mal-occlusion of the molars is present (*Fig.* 241). He is somewhat 'round-shouldered', though the curvature of the dorsal spine hardly amounts to a pathological kyphosis. The bones of the distal limb segments are disproportionately heavy and their prominences are accentuated. A skiagram of the hand shows the bones of a heavy, squared type, with definite 'tufting' of the terminal phalanges.

There is a marked hyperplasia of the connective tissue throughout the body. The dermis and subcutaneous tissue are generally thickened and inelastic; this is especially apparent in the face. The nose and lips are thickened; the features are heavy and coarse; a deep, permanent furrow crosses the brow transversely; the facial tissues have lost their natural resiliency, and expression is therefore inadequate. The hands are similarly affected; the fingers thick and square-ended, with heavy pads of inelastic subcutaneous tissue; the whole hand is broadened and the skin

of the palm deeply furrowed. The subcutaneous connective tissue of the feet is likewise thickened ; the toes are enlarged and clumsy and the feet broad ; there are prominent post-calcanean pads. The tongue is enlarged ; its motility is impaired by fibrous hyperplasia, so that the speech is thick and slurred. The hair is normal in quality, quantity, and distribution. There is profuse sweating of the palms and soles.

The blood-pressure is 118/80. The basal metabolic rate is +31 per cent. There is a definite history of glycosuria, but though he is at present on an unrestricted diet the glucose internal assimilation curve is normal. There is moderate enlargement of the heart ; other viscera appear to be normal.

Two pre-operative X-ray treatments, directed to the hypophysis, were given without affecting the constricted visual field peripheries in any appreciable degree.

Operation.—April 5, 1924. Dr. Cushing exposed the bulging sellar floor by the customary transphenoidal route. After removing the flakes of thinned bone and incising the tense dural capsule, soft adenomatous tissue was disclosed, and as much of it as was deemed safe was scooped away.

Fig. 242.—*Case* 6. Showing change in configuration of hands (pre-operative left ; post-operative right) after ten-months' interval.

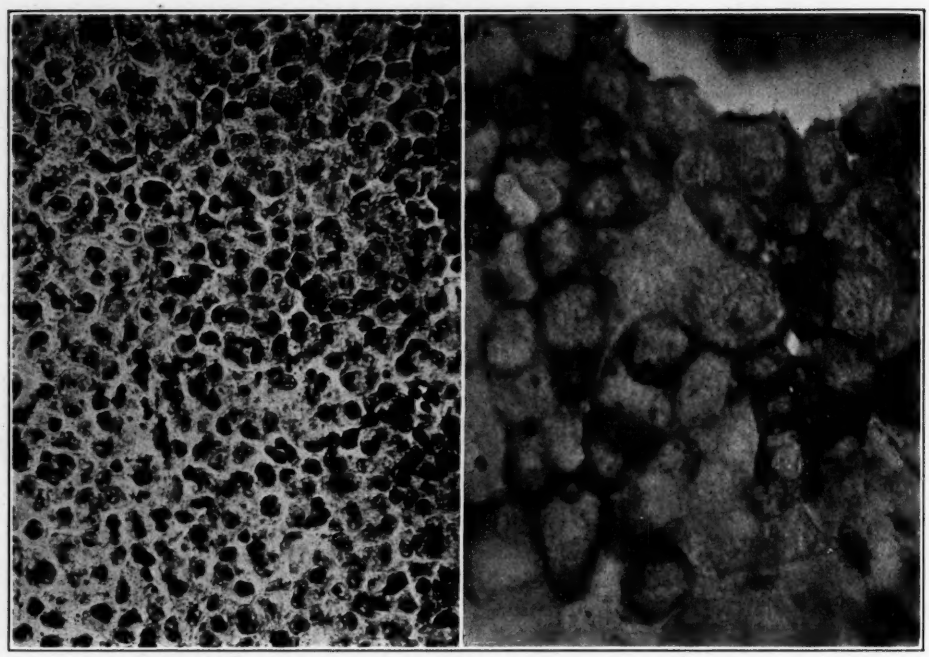
Post-operative Course.—A rapid and uneventful convalescence ensued. A third X-ray treatment was given before discharge. The headache, apathy, and somnolence were relieved. The visual acuity and fields showed no appreciable changes on his discharge on April 20 ; subsequent reports from his doctor recorded some improvement.

(The patient returned for examination on Feb. 25, 1925, ten months after his operation. He meanwhile had had thirteen X-ray treatments. There had been less improvement in vision than had been hoped for, and though the acuity had doubled on the right, the sharply cut hemianopsia persisted, and a restored patch of vision in the nasal field of the previously blind left eye did not help him greatly. But in other respects he had undergone an extraordinary change. This was chiefly noticeable in the subsidence of the pituitary 'myxœdema' or thickening of the soft parts. The change in his hands is shown by a comparison of the casts taken on the two admissions (*Fig.* 242) ; his shoes had become too large for him. There was, of course,

no change in the skeletal configuration, but he had lost about ten pounds in weight, his metabolism had gone down from +31 to +13 per cent, and his whole bearing was more alert and energetic.—P. B.)

PATHOLOGY.—The fragments of tissue are found to be composed of masses of polygonal cells (*Fig.* 243). They have no architectural arrangement. Blood-vessels are practically absent. The cells vary enormously in size, as do their nuclei. Almost a third of the cells have more than one nucleus, as many as six being present in some of them. The cytoplasm is packed with fine granules.

DIAGNOSIS.—Chromophile adenoma.



a *b*

FIG. 243.—*Case* 6. Photomicrographs of tumour. *a*. Hæmotoxylin and eosin stain. (× 300.) Note absence of connective tissue septa and presence of multinucleated cells. *b*. Neutral ethyl-violet-orange G stain. (× 850.) Only eosinophilic granules appear black in photograph. Granules very fine, making a poor photomicrograph.

The leading characters of the disease presented by this patient, in addition to the definite signs of local pressure, are: progressive structural deformity of the skeleton; hyperostosis; hyperplasia of the connective tissue throughout the body; significant recent gain in weight; asthenia; depression of sexual function; raised basal metabolic rate; hyperhydrosis; temporary glycosuria. This is a typical example of the acromegalic syndrome in a young adult accompanying which an eosinophilic adenoma is found.

C. MIXED ADENOMATA.

The Mixed Adenoma with 'Dyspituitary' Syndrome.—It has long been known that symptoms of the acromegalic and hypopituitary syndromes may be variously combined in the same individual. The hypopituitary symptoms in these cases have been variously interpreted. Tamburini supposed that they were due to a toxic product elaborated by the hypophysial tumour.

Others have attributed them to the consequences of necrosis or hæmorrhage in the adenoma or to pressure of the tumour on the base of the brain. Cushing[18] has assumed that just as a long-standing case of hyperthyroidism may occasionally show traces of myxœdema, so in hyperpituitarism evidences of lowered function might be superimposed on the fixed characters of acromegaly. His address before the Harvey Society in 1910 ended with the following paragraph :—

> It must be borne in mind, furthermore, that a hypophysial struma (adenoma), which at one time has represented a condition of functional hyperplasia, may in the end actually block or destroy the secretory possibilities of the gland. As a matter of fact it may be expected : (1) That in all cases of original hyperpituitarism associated with tumour, the functional end-result will be hypopituitarism ; and (2) That in many of the cases in which existing hypopituitarism is the striking feature traces at least of an early tendency to hyperpituitarism can be detected. These mixtures of the two syndromes of glandular over- and under-activity are most conveniently designated as dyspituitarism.

It should be pointed out, however, that, in many cases at least, the features of acromegaly and of the hypopituitary syndrome develop synchronously rather than in sequence. The distinct histology of the mixed adenoma, and the mixed nature of the associated glandular symptoms from an early stage of the disease, should be clearly recognized.

Some 13 of these mixed syndromes have occurred in the 162 cases that we have studied. The microscopic structure of the tumours found in these cases reflects the mixed character of the clinical syndrome. We will describe here one patient whom Dr. Cushing regarded as having a pure hypopituitary syndrome. Professor Biedl, who was visiting the clinic at the time, considered him to be acromegalic. The adenoma removed at operation in this case proved to be of mixed type.

Case 7.—*Surg. No.* 19907. **Adenoma with mixed syndrome. Transphenoidal operation. No improvement. Death six months later.**

Admission.—Oct. 17, 1923. J. M., age 19, single, a Jewish factory worker, referred by Dr. H. H. Beers, of New York City, complaining of failure of vision and headache.

Clinical History.—His early development was uneventful. He is the smallest member of his family, of whom none are large. Puberty was delayed and did not occur until his eighteenth year—two years ago. At this time he had a few nocturnal emissions at intervals of two or three months. Sexual libido was never pronounced. Shortly after the onset of puberty, nocturnal emissions ceased and his sexual desires were entirely lost. He failed to acquire the secondary masculine distribution of hair.

One year ago he experienced tenderness to pressure on the right eye. Six months ago he began to suffer from recurrent, dull, aching pain behind the right eye, followed a month later by frontal headaches of moderate severity. Four months ago vision began to fail bitemporally, and it has rapidly deteriorated, so that now he can read only large headlines. He has experienced no unusual thirst or undue frequency of urination. There has been no notable alteration in weight during the past four years.

Examination.—The following objective findings were disclosed : *Local.*—A bilateral primary optic atrophy ; V.O.S. 20/70 ; V.O.D. 20/200 ; bitemporal hemianopsia. The X rays show the sella turcica expanded, its floor depressed into the sphenoidal sinus, and its anterior and posterior clinoid processes eroded (*Fig.* 244).

General.—He is of average height, 171·3 cm., and weighs 64 kilo. His shoulders are narrow and his hips wide and rounded, resembling the feminine habitus (*Fig.* 245). The skin is very soft, fine, and smooth, like that of a child. The subcutaneous connective tissue of the lips, ears, and nose is thickened and inelastic, causing some immobility of these structures and giving to the features a certain coarseness. In the hands the subcutaneous connective tissue is thickened, forming well-marked pads on the palmar surface of the long fingers. The hair of the scalp is abundant, soft, and fine. He is quite beardless, and the axillary hair is absent. The pubic hair is scanty and is sharply limited above by a horizontal line and the genitalia are somewhat undersized. The basal metabolic rate is – 16 per cent. The fluid intake and output are normal during observation in the hospital. The urine is normal. A pre-operative X-ray treatment was given.

FIG. 244.—*Case* 7. Enlarged sella of mixed adenoma. (× 1.)

OPERATION.—Nov. 1. Dr. Cushing exposed the bulging and thinned sellar floor by the usual transphenoidal procedure. On incising the dura, soft, yellowish, œdematous tissue was exposed, and a considerable amount of it was spooned away.

Post-operative Course.—A rapid, uneventful recovery followed the operation. At date of discharge, Nov. 23, V.O.S. had improved to 20/30 while V.O.D. remained unaltered. A well-defined bitemporal hemianopsia remained. He still complained of mild, dull, aching pain behind the right eye. Two further X-ray treatments were given, and arrangements were made for them to be continued at intervals of about one month. Some weeks after his return home he had a series of convulsions in association with a local infection of the lip due to the retention of a piece of cotton-wool. He reported in person on March 24, 1924, his condition being practically unchanged. The results of the operation were therefore most disappointing, and

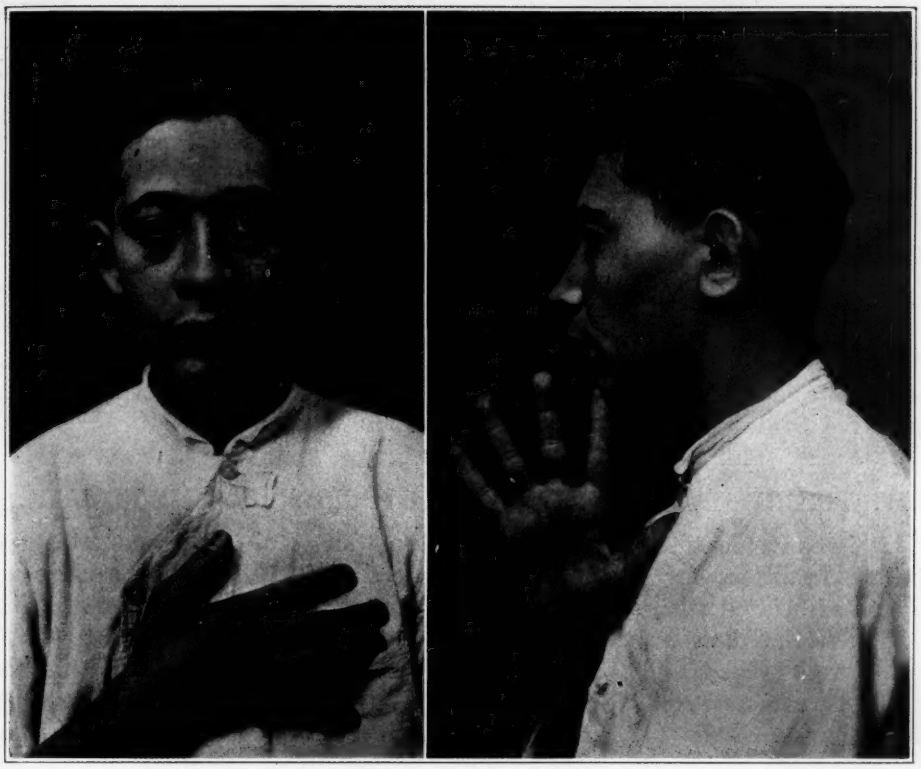
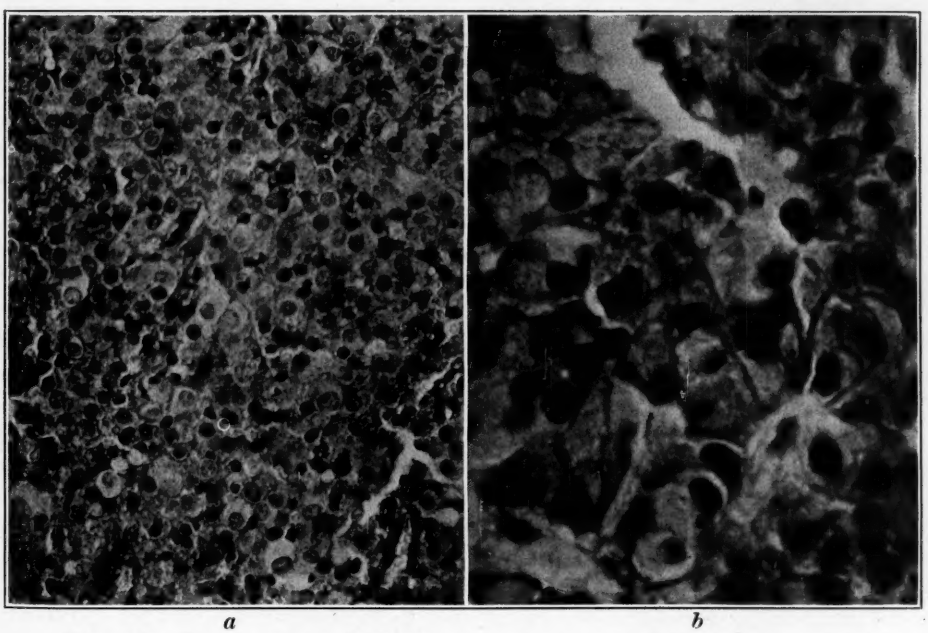


FIG. 245.—*Case* 7. Photograph of patient with ' mixed ' syndrome.



a *b*

FIG. 246.—*Case* 7. Photomicrographs of tumour. *a*. Hæmatoxylin and eosin stain. (×300.) Note absence of connective-tissue septa. *b*. Neutral ethyl-violet-orange G stain. (×850.) Note ring of granules in periphery of cells.

its primary object in improving vision had failed. Six weeks later he suddenly lost consciousness, and had a severe hæmorrhage from mouth and nose, with fatality in a few hours. A post-mortem examination was not made.

MICROSCOPIC EXAMINATION.—On superficial examination the tissue removed at operation resembles a chromophobe adenoma. The cells are elongated, with small single nuclei, and connective-tissue septa carrying small blood-vessels are frequent. However, certain areas are without adenomatous arrangement, and a specific stain shows a ring of eosinophilic granules in the periphery of most of the cells (*see Fig.* 223, *D* and *Fig.* 246). It must, therefore, be classified as an adenoma of mixed type.

The outstanding characters in this case were: a mixed type hypophysial adenoma; signs of local pressure; depression of sexual function; delayed puberty; hypoplastic character of skin and hair; slight skeletal build; undersized genitalia; and a certain amount of connective-tissue hyperplasia giving suggestive evidences of overgrowth in lips, nose, and hands.

IV. THE SYMPTOMATOLOGY OF HYPOPHYSIAL ADENOMATA.

It is convenient to discuss the symptomatology of the adenomata under separate headings, for the reason that certain of the symptoms and signs may be associated with a pituitary tumour of any sort, while others fall into groups associated with specific types of adenoma. We shall discuss: (1) *The local pressure effects of the tumour;* (2) *The signs of general intracranial tension to which it may give rise;* (3) *The peculiar features of the hypopituitary syndrome;* (4) *The constitutional disturbances of the acromegalic syndrome;* (5) *The constitutional features of the mixed syndrome.*

1. **Local Pressure Signs.**—These are common to all pituitary adenomata which attain sufficient size to produce them.

Headache.—This, as Dr. Cushing has suggested, is in most cases due to stretching of the dural capsule. It is typically a dull, aching pain, or a sensation of pressure and discomfort, referred to one or both temples or behind the eyes. This discomfort is often an early symptom, and may have entirely subsided by the time the sella has become widely distended. When it persists, it is usually completely relieved by a sellar decompression.* A subtemporal decompression, on the other hand, which usually relieves the headaches of other forms of intracranial tumour, has no effect on pituitary headaches.

Roentgenological Signs pertaining to the Sella.—For a satisfactory examination stereoscopic radiography should be employed. The sella which contains an adenoma is characteristically expanded by pressure from within—it is 'ballooned'. Examining the sellar boundaries *seriatim* one notes: The anterior clinoid processes are characteristically thin and pointed, being scalloped out on their lower surfaces; one process may be more affected than the other, thus giving an indication of the direction of extension of the tumour; in long-standing cases the two processes may be separated by an

* This, perhaps, does not apply so certainly to the persistent headaches which sometimes accompany acromegaly and which must be due therefore to some cause other than capsular distention.

interval wider than is normal; they may be entirely obliterated by pressure atrophy. The floor of the sella is typically depressed into the sphenoidal cell; its outline is commonly clear, smooth, and thin; occasionally it may be rendered irregular by the presence of supporting septa in the sphenoidal cell; in long-standing cases it may be partially eroded by pressure atrophy. The dorsum sellæ and posterior clinoid processes are usually much thinned, but they maintain with the outline of the expanded sellar floor a continuous curve; in long-standing cases they may be entirely eroded by pressure atrophy or so nearly so that several exposures may be required before the thin remaining scale of bone is caught on edge by the rays and becomes visible on the film.

We wish to emphasize that the characteristic appearances are those of an even, more or less globular expansion of the sella. So typical of an hypophysial adenoma is this appearance that the great majority of them can be differentiated thereby from other lesions distorting the sella. Of these, the craniopharyngeal pouch cyst is perhaps the most common. As a rule these tumours are extra-sellar in origin, and though they distort the sellar outlines, the radiological picture is distinctive even in the absence of the customary shadows of calcareous deposits[20]. Moreover, these congenital cystic tumours usually give symptoms early in life, and only when one of them actually arises within the sella itself and remains free from calcareous depositions does the sellar deformation resemble that produced by an adenoma. Only two or three cases of this sort have occurred in Dr. Cushing's entire series. The sella may undergo pressure absorption from other conditions, from suprasellar meningiomata, for example, and more particularly as a late change when there is a marked and long-standing internal hydrocephalus; but experience should make it possible to distinguish the sellar changes produced by these lesions from those of the average adenoma unless the condition is so advanced as practically to obliterate all outlines of the fossa.

Optic Changes.—Distortion and compression of the chiasm and optic nerves, with a primary optic atrophy, is one of the early consequences of any hypophysial tumour. Later, if the neoplasm bursts through the capsule and reaches such proportions as to raise the intracranial tension by its actual bulk, which it rarely does, or by causing a secondary hydrocephalus—also a rare event—a definite 'choking' of the optic disc may be superimposed on the primary atrophy.

Projecting upwards, in the mid-line as a rule, the tumour implicates the chiasm in the first instance, and causes a bitemporal defect of the visual fields. The very typical manner in which a superior bitemporal notch first appears, and extends round the circle of each field, implicating in turn the upper temporal fields, the entire temporal fields, the lower nasal quadrants, and lastly the upper nasal quadrants, to total blindness, has been fully described by Cushing and Walker.[21] After the chiasm has been released from pressure, this process is exactly reversed (*Fig.* 247). The relationship of this sequence of events to the internal architecture of the optic nerves, chiasm, and tracts has also been fully discussed by these authors. While this is the usual type of visual disturbance, homonymous visual defects from lateral pressure on the chiasm, or impairment of one eye alone from implication

of one of the optic nerves, are not very rare; and innumerable combinations and varieties of these lesions may be encountered. The visual disturbances are the most frequent cause of the patient's seeking medical advice.

If the growth continues to enlarge it may reach enormous proportions, and in the course of the disease give rise to other local manifestations of pressure. Paresis or paralysis of the *oculomotor*, *abducent*, and *trochlear*

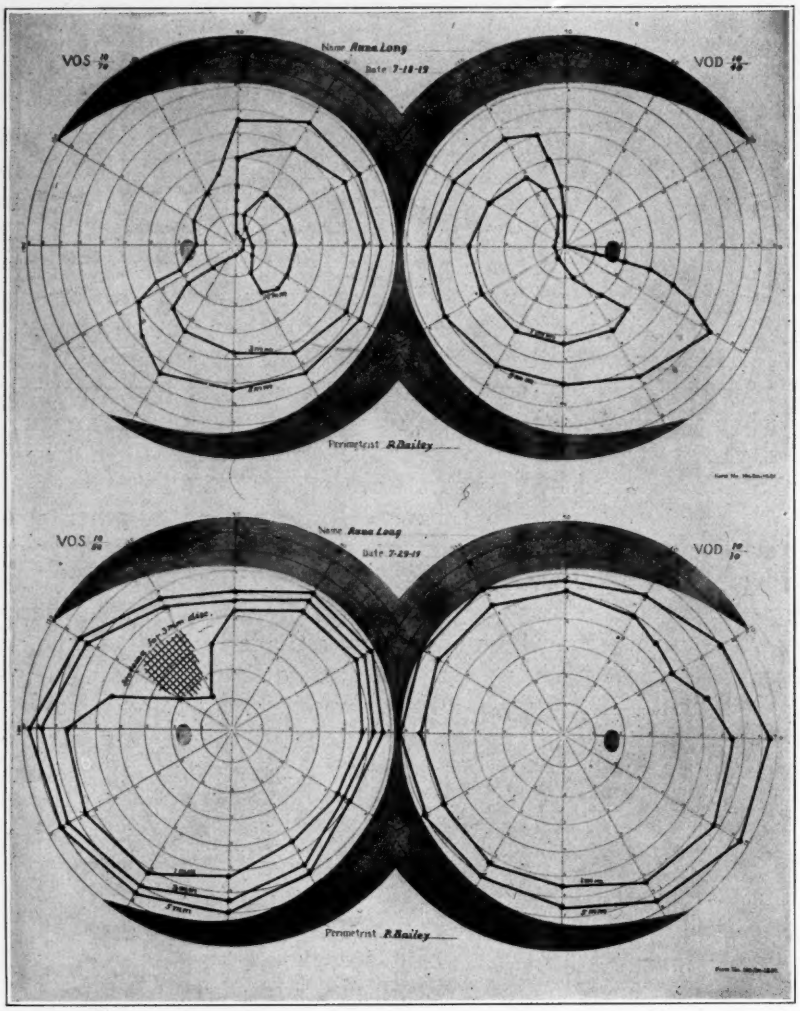


FIG. 247.—Visual fields to show improvement after transphenoidal operation. Pre-operative above; post-operative below. Operation performed July 19, 1919.

nerves may result therefrom. All combinations of paralytic strabismus, pupillary dilatation, and ptosis may be encountered in advanced cases. Occasionally the obstruction to the venous circulation from pressure on the cavernous sinuses causes œdema of the eyelids and obvious *congestion* of the venules of this region. A unilateral or bilateral *exophthalmos* may also result. These are late and inconstant evidences of a hypophysial tumour.

As the tumour distends the sellar floor and bulges into the sphenoidal sinus, congestion of the mucous membrane may cause *epistaxis*, but this is usually very small in quantity, merely staining the handkerchief from time to time. The deformity of the sphenoidal sinus may interfere with the proper evacuation of its secretions and a mild inflammatory condition of the mucous membrane may be induced, with retention and periodic evacuation of its contents, causing post-nasal dropping. There may be some consequent disturbance of the sense of smell, but *anosmia* from pressure implication of the olfactory nerve is comparatively rare. When present it is much less suggestive of an adenoma than of a meningioma, a form of tumour which has a predilection for the meninges of this region.

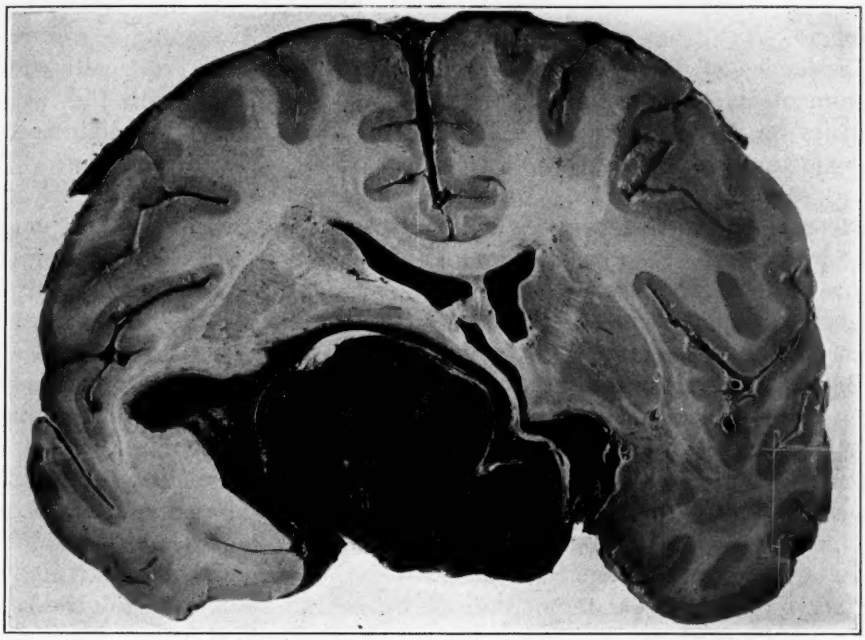


FIG. 248.—Adenoma from a case of acromegaly. M. van W., *Surg. No.* 1784. Note the great distortion of the basal region of the brain.

Should the adenoma rupture its capsule and extend upwards into the cranial chamber in the median line, it may press upon and deform the hypothalamic region of the brain, and cause polyuria and polydipsia; but as a matter of fact these symptoms, which in exaggerated form constitute *diabetes insipidus*, are an infrequent consequence of pituitary adenoma. This disorder is to be sharply distinguished from the polyuria which occurs in association with the glycosuria of acromegaly, and which fluctuates with the sugar output just as in diabetes mellitus. As the uncinate region of the temporal lobe is subjected to pressure by lateral enlargement of the adenoma, typical *uncinate* attacks may occur—hallucinations of smell, usually of disagreeable odours; but this, too, is a rare symptom of hypophysial adenomata.

In extreme cases (*see Fig.* 248) the adenoma may protrude still further

into the cranial cavity, largely obliterating the cavity of the third ventricle and compressing the basal cerebral nuclei. *Drowsiness* and somnolence passing on to varying degrees of *coma* are common signs of such gross intracranial protrusions. The tumour may actually reach the level of the foramina of Munro and induce an acute obstructive hydrocephalus with general pressure symptoms.

2. **General Pressure Signs.**—Evidences of an increased intracranial tension are usually terminal features of hypophysial disease. They arise either on account of the actual bulk of the intracranial protrusion, or, as just mentioned, by virtue of a complicating obstructive hydrocephalus. Headache, vomiting, and choked disc superimposed on the already atrophic nerves are the leading signs, and their significance is peculiarly grave

3. **The Constitutional Disturbances peculiar to the Hypopituitary Syndrome.**—

Depression of Sexual Function.—This is the first and practically constant symptom of the chromophobe adenoma, and is consistent with the fact that necropsies on these cases may reveal (apart from the hypophysial neoplasm) nothing of note except an atrophy of the gonads. Our most accurate index of its onset is amenorrhœa. Depression of libido sexualis, especially in the celibate male, may not be very apparent to the patient himself, though in a large proportion of our male cases loss of libido is one of the early symptoms to be recorded. In women, however, the cessation of the menses invariably attracts the patient's attention, and the constancy of amenorrhœa as the earliest symptom is remarkable.

Of all the female cases between the ages of 20 and 40 years in the series, there are but two exceptions to this rule. One of these was complicated by the presence of hyperthyroidism, and the basal metabolic rate was +22 per cent. Even in this woman, age 32 years, the menses had been irregular and scanty since their onset at the age of 16 years, and complete amenorrhœa developed shortly after the appearance of the local manifestations of hypophysial tumour. Whether the co-existence of hyperthyroidism had any influence in maintaining menstruation, we cannot tell. In the other exception to which reference has been made, a woman of 31 years, menstruation remained regular with but two lapses—once in 1916 and again in 1922, when a single menstrual period was three weeks late in its appearance, though local signs of hypophysial tumour had been present for many years. Following the transphenoidal operation for the relief of local pressure signs complete amenorrhœa developed.

It is characteristic of the amenorrhœa of the hypopituitary syndrome that it is of gradual onset. Complete amenorrhœa is usually preceded by a variable period of irregularity and paucity of the flow. Operative intervention, which usually consists in partial removal of the tumour combined with a sellar decompression, generally has no influence upon the existent depression of sexual function. In the series there is but one notable exception to this rule. A woman, age 27, with typical amenorrhœa and other hypophysial manifestations of a typical chromophobe adenoma, was operated upon by the usual transphenoidal procedure and was put on a course of glandular (anterior lobe) therapy. Five months later, regular menstruation returned.

Six months thereafter, she became pregnant, and in due course was delivered of a normal child.

Atrophic Changes in the Skin and Hair.—Atrophic changes in the skin and hair are, in our own experience, as constant signs of the chromophobe adenoma as is sexual depression. They are minor changes and occasion no inconvenience to the patient, and they must be carefully sought by the observer. For these reasons any attempt at a statistical review of them would be unreliable and fruitless, and no opinion can be formed of the time of onset of these changes relative to other symptoms. In our personal experience we have encountered but one case in which they were entirely absent (cf. *Case* 1). Their character varies somewhat with the age of the patient. In the adolescent the skin is like that of a little child—thin, delicate, smooth, and practically hairless. In the adult the skin is again thin, delicate, smooth, and usually unduly dry. The hair of the head is of normal quantity, but of a fine, soft, dry texture. The facial, axillary, and pubic hair is apt to be scanty, and the distribution of the latter is of the feminine type. Hair is much diminished or absent over the remainder of the trunk and over the limbs. From the age of about 35 onwards, the skin, which is still soft, thin, and delicate, becomes finely wrinkled. This fine wrinkling is a very characteristic appearance; it is well shown in *Fig.* 234. At all ages there is a very definite lack of the fibrous tissues of the cutis, secretion of sweat is diminished, and the hair is scanty and atrophic.

Adiposity.—This is a fairly common symptom in the hypopituitary syndrome. Among the younger patients it is definitely present in at least 80 per cent of the cases; but it may be entirely absent. Among the older patients it is less manifest, being present in about 50 per cent. Apart from actual pathological adiposity at the time of examination, previous unaccountable fluctuations in the patient's weight are of significance. In patients showing no particular obesity at the time of examination, it is quite common to obtain a history that within the past few years there had been a sudden gain of some 10 or 15 kilo., which was subsequently lost. Except for the unusual pallor of the skin there is nothing particularly characteristic about the adiposity of pituitary disease to distinguish it from adiposity due to other causes; but the history of sudden fluctuations in weight, whether maintained or not, is very typical. Unlike other victims of adiposity, these people are apt to suffer from the cold.

The Basal Metabolic Rate.—This is usually low in the hypopituitary syndrome. It is never above normal. It varies between about – 5 per cent and – 35 per cent from normal. We do not consider a reading which falls within 10 per cent of the normal standard to be of pathological significance, and a considerable number of cases come within this limit. The average, however, is about 20 per cent below normal. The low basal metabolic rate, no doubt, accounts for the lethargy and inactivity with slow pulse and slightly subnormal temperature which the majority of these patients exhibit.

Infantilism.—Infantile characters are not typical of hypophysial adenomata, for the reason that the tumour is very rare during the pre-adolescent period of life. In two cases (cf. *Case* 2) in which there was a suggestion of infantilism, it was of slight degree, because the patients were well advanced

toward adolescence when the disease affected them. We know of no recorded case of hypophysial adenoma in which infantilism was a striking feature.* This is in marked contrast to the syndrome accompanying the craniopharyngeal pouch cyst of developmental origin, which usually manifests itself in childhood and is associated with a very striking degree of infantilism.

Carbohydrate Tolerance.—Since attention was first drawn to the subject by Goetsch, Cushing, and Jacobson,[22] much has been written on carbohydrate tolerance as affected by hypophysial disease, especially in those types with which we are now dealing. Before the days of clinical calorimetry, a study of sugar tolerance was about the nearest approach one had toward an estimate of the metabolism of these patients. Individuals were said to have 'a high or low carbohydrate tolerance', depending upon the amount of glucose they could ingest without manifesting glycosuria. It was assumed when tolerance was high, as is usually the case in hypopituitarism, that the patients possessed an abnormal facility in transporting, modifying, and storing glucose in their bodies. In order to avoid the uncertain factor of alimentary absorption in this test, we have carried out intravenous administration of glucose in a number of cases. This we term the internal glucose assimilation test.

Contrary to the former belief in a 'high glucose tolerance', we find that the blood-sugar curve is considerably longer in returning to its basal level in these individuals than in normal persons—i.e., their capacity for dealing with glucose in the blood-stream is subnormal. One can only conclude from this observation that the alimentary test, although useful as a clinical investigative procedure in hypopituitarism, has proved misleading from a physiological standpoint. It appears probable that absorption from the alimentary canal is so slow in them that even their retarded biochemical mechanism can keep the blood-sugar level below the 'kidney threshold' for glycosuria. It is quite probable that the retardation of both processes—alimentary absorption and internal distribution—merely reflects the lowered metabolic rate which we know these patients have. Naturally, in connection with the hypopituitary syndrome glycosuria never occurs—in contrast, as we shall see, to the findings in acromegaly.

4. **Constitutional Disturbances peculiar to the Acromegalic Syndrome.**—*Depression of Sexual Function.*—It will be noted that depression of sexual function is a symptom common both to the hypopituitary and acromegalic syndromes. On the average it is probably one of the earliest symptoms in both disorders, but the histories of the acromegalics record many exceptions, and in some cases menstruation and libido sexualis have persisted for many years in the presence of a well-marked acromegalic symptomatology.

Connective-tissue Hyperplasia. — Hyperplasia of the connective tissue of the body is a constant and essential element of the disease. It is especially evident in the subcutaneous tissues of the lips, nose, scalp, hands, and feet, which become markedly thickened and their consistence stiff and inelastic. The dermis itself is thickened, and gives to the skin a coarse appearance and texture which is associated with considerable œdema. The visceral enlargement that is present in advanced cases is due to hyperplasia of their

* Cf. footnote, p. 330.

connective-tissue elements. The neuritic pains from which these patients suffer are probably due to the fibrous hyperplasia which is present in the nerve sheaths as well as to the narrowing of the intervertebral foramina from hyperostosis. The large, stiff, clumsy tongue of acromegaly is another example of fibrosis.

Changes in Skin and Hair.—As just mentioned, the skin becomes thick and coarse from fibrous changes. In certain parts of the body, such as the palms of the hands and the scalp, it may be deeply corrugated, giving occasionally a very remarkable appearance upon the scalp, which Dr. Cushing speaks of as "the bull-dog scalp of acromegaly" (*Fig.* 249). There is apt to be profuse sweating, often accompanied by a disagreeable odour. Hypertrichosis occurs sometimes to a remarkable degree, though this is by no means constant. All this is in marked contrast to the delicate, dry skin which accompanies the hypopituitary syndrome.

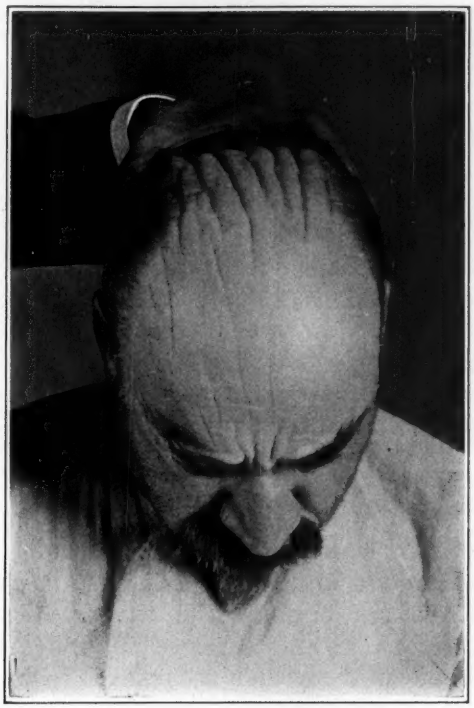


FIG. 249.—To show the furrowed scalp sometimes seen in acromegaly. A. C., *Surg. No.* 4215.

The Osseous Changes.—These are the outstanding features of the disease. The skeletal deformities tend to increase as time goes on, and of course remain permanent, even should the period of hyperpituitarism lapse. Hence, so far as these manifestations of the disease are concerned, the expression "once an acromegalic, always an acromegalic" applies. We need but mention the well-known enlargement and deformities of the bones of the face, the huge air sinuses, the undershot jaw with its wide angle; the upper dorsal kyphosis; the enlarged clavicles and ribs; the hyperostosis of the terminal phalanges of the fingers, and of the limb bones and vertebral column.

The Basal Metabolic Rate.—This is much less constant in acromegaly than in the hypopituitary syndrome. As a rule it tends to be elevated in the active periods of the disease, as in the case recorded (*Case* 6), and though registrations of + 30 per cent are not infrequent, it never attains the high figures seen in extreme cases of hyperthyroidism. On the contrary, normal or subnormal registrations are not uncommon.

Glycosuria and Carbohydrate Tolerance.—About 20 per cent of the acromegalics in the series have shown spontaneous glycosuria in greater or lesser degree. The glycosuria is characterized by its extreme variability from time to time in the same individual. At one period—usually after the disease is well established—it may be a prominent symptom, accompanied

by polyphagia, polyuria, and loss of weight. A few weeks later both it and its associated symptoms may have entirely disappeared. It is a common experience, with cases of acromegaly which are under observation, to discover spontaneous glycosuria on one or two isolated occasions. The glycosuria of acromegaly is certainly of a diabetic nature—i.e., it is due to a failure to utilize glucose in the body—but whether it is actually pancreatic in origin is undetermined. In this clinic one case died in typical diabetic coma, and glycogen was identified in the liver post mortem, in approximately normal amount.

We have not had the opportunity personally to investigate the 'carbohydrate tolerance' of an acromegalic who had glycosuria, but it is presumably low. In several who had not glycosuria the 'internal glucose assimilation curve' was within normal limits.

5. **The Constitutional Features of the Mixed Syndrome.**—Though the patients of this category present no symptoms other than those mentioned above in the acromegalic and hypopituitary syndromes, the symptoms of the two disorders are variously combined. The fat, hypotrichotic individual who at the same time has enlarged accessory nasal sinuses, some exaggeration of the supra-orbital ridges and of the various prominences of the limb bones, and is perhaps overgrown, is typical of the mixed class. It should be clearly understood that many cases which, on account of a marked preponderance of one or the other syndrome, are commonly relegated to that particular class, may yet be tainted by traces of the other. For example, the patient portrayed in *Case* 5 whom we selected to typify acromegalic gigantism was almost beardless at the age of 21.

V. PHYSIOLOGICAL CONSIDERATIONS.

To construct physiological theories from pathological findings is always hazardous, and it is especially so in regard to pituitary disorders, but so much stress has been laid in the preceding sections on the distinction between eosinophilic and chromophobe adenomata, and the correlation which exists between them and the clinical picture, that we are obliged to discuss the implications of this distinction, especially since we are dealing with a tumour of a glandular organ.

Contrary to the opinion of Sjövall[23] and others, the symptoms of pituitary disease have been, and must continue to be, interpreted in the light of animal experimentation rather than by deduction from the pathological findings in clinical cases, and especially is this true in cases of tumour and hydrocephalus, as one of us has already pointed out,[24] where the normal anatomical relations are enormously distorted. However, certain definite suggestions emerge from the clinical pathology. We shall consider the problem illuminated from this source alone in the first place. We shall then consider it in the light of both clinical pathology and experimental evidence.

From the facts furnished by pathological states, we should be led to consider that the normal hypophysis may be concerned with growth, with sexual function, with the condition of the skin and hair, and with the basal metabolic rate, since changes in these almost invariably follow upon destructive compression of the hypophysis by an adenoma (or other neighbouring

tumour). Nevertheless, we are faced with certain exceptions which require explanation; and we can obtain little evidence as to which part of the hypophysis is concerned. We should also surmise that adiposity, hyperplastic changes in the bones and connective tissues, polyuria, and glycosuria were due to some cause other than compression or destruction of the hypophysis, as they are present in only a variable proportion of cases.

Such conclusions, however, require careful investigation. We realize at once that, in addition to destruction of the pituitary gland, a complicating factor exists in that an adenomatous neoplasm is present which may or may not furnish a normal or a perverted hypophysial secretion.

Let us first eliminate from the category of possible manifestations of hypophysial destruction the symptoms which there is reason to believe are due to another cause. The hyperostoses and connective-tissue changes of acromegaly are constantly associated with an eosinophilic adenoma; they never accompany an anatomically similar tumour which is not eosinophilic; they are associated with no other constant pathological lesions. Acromegalic gigantism is dependent on the eosinophilic adenoma for the same reasons, in those cases in which the development of the eosinophilic adenoma has preceded the cessation of growth of the individual. Other factors, such as the site, size, and local effects of an adenoma being equal, the 'eosinophilia' of the tumour remains alone to account for these symptoms of acromegaly and of gigantism.

Let us now consider if any symptoms can be etiologically attached to a destructive lesion of the hypophysis from the evidence of clinical pathology. Depression of sexual function is a feature almost constant for all types of pituitary adenoma, and as it occurs so early as to preclude the factor of hypothalamic injury as a cause, we are left with two possibilities: (1) That all forms of adenoma produce some 'toxin' capable of depressing sexual function; (2) That destruction of the hypophysis or diminution of its secretion is responsible. Exceptions to the rule that depression of sexual function is the first symptom have occurred in but two cases of chromophobe adenomata. On the other hand, with eosinophilic adenomata early amenorrhœa is less constant. The only symptoms, however, which may precede amenorrhœa are the acromegalic changes in the bones and connective tissues, which, as we have seen, are probably due to the active secretions of the tumour, and are certainly not the consequences of local pressure of the tumour upon the hypophysis. In these cases amenorrhœa constantly precedes signs of local pressure, such as optic atrophy, just as it does in the cases of chromophobe adenomata. We must therefore conclude that an eosinophilic adenoma may induce the constitutional changes of acromegaly, by its secretory activity, before it has attained a size sufficient to cause depression of the function of the hypophysis by pressure. This further indicates that amenorrhœa is probably an early consequence of tumour pressure—that it is due to depression of the function of the pituitary gland, and is not a result of secretory activity nor of toxin production by the neoplasm.

We are unable to apply to the cutaneous changes of the hypopituitary syndrome the same line of argument as in the case of amenorrhœa, because it is impossible to determine accurately their time of onset. They are a

practically constant accompaniment of the chromophobe adenoma, and rarely occur with the eosinophilic tumour, which, on the contrary, causes excessive growth of hair and thickening of the skin. This suggests that the cutaneous changes of the hypopituitary syndrome are due to a loss of function, while the eosinophilic tumour prevents these effects of pituitary lesion by producing acromegalic changes by means of its own secretory activity.

The basal metabolic rate is constantly lowered with chromophobe adenomata, while it is often raised with eosinophilic adenomata. It is possible that the same line of reasoning applies as in the case of cutaneous changes.

Concerning the remainder of the clinical symptoms we can say little from the evidence derived from clinical pathology. It should also be noted that little concerning the functions of the individual parts of the hypophysis can be learned from this source.

So far we have restricted ourselves to the clinical pathology of hypophysial adenomata as an approach to the elusive physiology of the pituitary gland. A more fruitful and a surer way exists in the application of the evidence furnished by experimental research to a critical interpretation of the clinical data. It would be out of place to enter here into a full discussion of the experimental work bearing on pituitary physiology, but we may recapitulate our present views. Some time ago one of us, in approaching the problem from the experimental standpoint, recorded the following conclusions:[24] "(1) The pars anterior (pars distalis, vorderlappen) of the hypophysis is in its histological structure glandular. Its secretory product has not been isolated, and the effects which it exerts on the organism are not conclusively demonstrated; (2) The pars posterior (pars intermedia and pars nervosa) is structurally not glandular (in dog and man). Its removal from the organism (dog) gives rise to no symptoms". In the light of experimental evidence obtained since these conclusions were recorded the first requires amendment. It had already been shown by Fichera, Cushing, Aschner, and others that removal of a large part of the gland, including the anterior lobe in a growing animal, resulted in dwarfism. Smith and Graeser[25] have shown also that in the rat the pars distalis exerts a definite influence upon growth, and that extensive injury of the pars anterior results in dwarfism and infantilism, which can be overcome by the intraperitoneal administration of extracts of the pars distalis of the beef hypophysis. It is highly probable, therefore, that the rare infantilism and dwarfism occurring with chromophobe adenomata (and much more often with the suprasellar tumours) is due to depression of function of the pars distalis of the hypophysis.

This brings us to an interesting point which may elucidate some of the more obscure symptomatology. The eosinophilic adenoma, in spite of the fact that it depresses or eliminates the function of the normal hypophysis, yet induces gigantism when acting within the growth period. Here we have an example of a tumour interfering with an important physiological function, and in all probability substituting for that function the effects of its own secretory activity, which must be very similar to those of the normal gland. In other words, dwarfism should result from hypophysial destruction; but instead, the activity of the eosinophilic tumour prevents this effect and causes gigantism. Evans and Long[17] have produced gigantism in rats by suitable

administration of pars distalis preparations, and in this respect the effects of the eosinophilic adenoma are at least akin to the experimental hyperpituitarism thus produced. It is consistent to link with this similarity in biological activity the close histological resemblance of the eosinophilic tumour to the normal gland. We would further deduce from these premises that the eosinophilic granules of the normal gland are probably concerned with the growth of the organism.

When, however, we attempt to correlate acromegalic changes (as contrasted with simple gigantism) with experimental physiological findings we meet with difficulties, for acromegaly has as yet no experimental counterpart. In the present state of our knowledge, it is profitless to speculate upon the possibility as to whether the eosinophilic adenoma produces an excessive or a perverted secretion to account for the changes of acromegaly.

A word may be added concerning the pars posterior of the hypophysis. No physiological activity has been demonstrated from it in mammals, either experimentally or clinically, though numerous pharmacological activities have been obtained from its extracts. Its total ablation in the dog causes no symptoms, as many investigators have shown, and we suspect that its compression by a tumour in man causes no symptoms. At any rate, it probably plays no part in the symptomatology of the hypophysial tumours which we are considering.

Polyuria and polydipsia are so rarely seen with hypophysial adenomata, except for the polyuria accompanying the diabetes mellitus occasionally occurring in acromegaly, that they need not be discussed, except to note that if the essential lesion of diabetes insipidus be considered to lie in the pars posterior of the hypophysis, it is strange that it occurs so rarely with an intrasellar tumour such as the hypophysial adenoma.

VI. DIFFERENTIAL DIAGNOSIS.

The recognition of a tumour of the hypophysial region presents little difficulty as a rule. The primary optic atrophy, characteristic visual field defects, the ocular palsies, the X-ray picture of sellar deformity, leave little room for doubt. It is essential, however, to carry the diagnosis a stage further, and to be able to form an opinion as to whether the tumour is or is not an adenoma, since from a surgical standpoint the correct differentiation of the adenomata from the various parahypophysial lesions is of the first importance.

The eosinophilic adenoma is not likely to be confused with any other lesion, as the signs of acromegaly or gigantism with which it is associated are almost unmistakable. The chromophobe tumour, on the other hand, may be easily confused with a number of parahypophysial lesions, since simple compression of the pituitary gland and neighbouring nerves are common to all of them. The more important of them are the suprasellar cysts originating from Rathke's pouch, suprasellar endotheliomata, teratomata, cholesteatomata, gliomata of the optic chiasm, and even hydrocephalus. Each of these conditions may be associated with the hypopituitary syndrome, probably by virtue of the common factor of compression of the pituitary gland. They

may all induce signs of compression of the nerves of the region which would be compatible with adenoma.

By far the commonest of these parahypophysial lesions are the congenital craniopharyngeal pouch tumours. Fortunately, as already mentioned, these lesions show in 85 per cent of the cases a definite and typical shadow in the X-ray by reason of calcific deposits. These cases consequently will rarely cause confusion, though an isolated fragment of a posterior clinoid process lying over a sella which has been extensively eroded by an adenoma may sometimes simulate a patch of calcification in such a tumour. The 15 per cent of Rathke's pouch cysts which are not calcified, and the rarer suprasellar endotheliomata, teratomata, and cholesteatomata, are less readily distinguished from the chromophobe adenoma. Two factors are of especial value in diagnosis: (1) The different character of the sellar deformity or the absence of deformity, as revealed by the X rays; (2) The character of the visual field defects, which are apt to be less regularly bitemporal, possibly from the circumstance that the adenoma exerts pressure on the chiasm from below, while the suprasellar tumours encroach upon it from behind or above. Moreover, the parahypophysial tumours are much less constantly median in their location. They are apt to cause field defects which are irregular, and which often affect the lower quadrants before the upper. The adenoma pressing from below usually causes a bitemporal defect which primarily involves the upper and outer quadrants. These are suggestive points, but are not constant either for adenoma or for suprasellar tumour. A tumour in this neighbourhood which causes an homonymous defect in vision or a defect of irregular disposition is more likely to be parahyphophysial than adenomatous. The adenoma is very rarely encountered below the age of 20 years, while most pharyngeal pouch cysts are seen below this age. In doubtful cases, therefore, a consideration of the patient's age may be important.*

In gliomas of the optic nerve or chiasm the field defects are atypical, and a localized erosion of one or both anterior clinoid processes as disclosed by X rays may aid in the differential diagnosis. These lesions, moreover, are rare, and represent less than 1 per cent of all intracranial tumours, as stated in a report from this Clinic dealing with this special subject.[26]

Though hypophysial symptomatology associated with hydrocephalus is apt to be slight and late in appearance, the dilated third ventricle may cause a pressure absorption of the sella which is very misleading. It is remarkable that symptoms of a suprasellar cyst which happens to cause hydrocephalus should be difficult to distinguish from those caused by a cerebellar tumour. This, however, would hardly apply to the symptomatology for adenomata.

Thus, in the vast majority of cases, the pituitary adenoma can be readily differentiated from the conditions which simulate it. Only when the disease

---

* Since this paper was written two children about 14 years of age entered the Clinic at about the same time, typical examples of pituitary infantilism of the adipose type. Both had bitemporal hemianopsia, optic atrophy, and ballooned sellas of the adenoma type. One of them proved to have an intrasellar tumour of Rathke's pouch origin, the other a typical chromophobe adenoma.—P. B.

is so advanced as to cause complete blindness and complete obliteration of the sellar outline in the absence of calcification, so that all distinctive features are lost, do great diagnostic difficulties present themselves. Fortunately to-day such cases are rarely encountered.

VII. TREATMENT.

The most grave and distressing of the symptoms are those due to local pressure of the neoplasm, in so far as it produces headache and affects vision. It is to alleviate if possible these mechanical effects of the lesion that the present-day operative measures have been devised. We have also to consider the constitutional symptoms, which are due on the one hand to loss of function and on the other to excessive function. The first naturally suggests replacement by organotherapy; the second, if we are to draw further analogy from our experiences with diseases of the thyroid, suggests the diminution of functional activity by some destructive procedure, surgical or otherwise. At our disposal for therapeusis we have, therefore: (1) *Physiotherapy*—X-ray treatment; (2) *Medical therapy*—the administration of drugs; and (3) *Mechanical therapy*—surgical procedures.

Radiotherapy.—It is well known that X rays have a specific destructive influence upon certain neoplastic cells. This activity can be employed to advantage in dealing with hypophysial adenomata. The work of Béclère[27] first established X-ray treatment of pituitary tumours on a firm basis. As knowledge of radiotherapy has advanced his original technique has been considerably modified. At this Clinic* X-ray treatments for pituitary adenomata are given at intervals of three weeks. The rays are directed to the pituitary fossa through three portals of entry. Areas $3\frac{1}{2}$ in. square over the temporal bone on each side and occasionally a similar frontal area are used for this purpose. The treatments consist in a maximum skin dose at each sitting, and are composed of approximately the following factors for the ordinary 10- or 12-in. X-ray machine:—

Spark gap ..	9 to 10 inches
Voltage	80,000 to 100,000 volts, v.m.s.
Distance (target to skin) ..	12 inches
Filter	0·25 mm. of copper and one thickness of sole leather
Time	30 minutes
Amperage ..	5 milliampères

This usually causes an epilation of the areas treated, but rarely an erythema. Treatment through one area is not repeated at an interval of less than three weeks. Two or even three treatments may be given through separate portals at one sitting with but slight immediate reaction—mild headache, general malaise, and occasionally vomiting. It is our practice, however, to give single treatments on succeeding days, the patient remaining in the Hospital during the intervening twenty-four hours.

---

* We are indebted to Dr. M. C. Sosman for this description of the technique which he follows at the Brigham Hospital.

From an experience of 53 cases at this Clinic, in which between four and eight 'series' of treatments were given, it appears certain that the growth of the tumour may usually be retarded, and an actual reduction in its size sometimes effected, by radiotherapy. It should be mentioned, however, that the treatment is not entirely free from risk (cf. *Case* 5). In two of the 53 cases temporary aggravation of their symptoms was observed. Sudden and severe headache followed the treatments, they suffered from increased difficulty of vision, and from general lassitude and prostration. One of them was subsequently completely relieved by a sellar decompression operation. In the other the symptoms subsided spontaneously forty-eight hours after treatment, apparently consequent on a rupture of the tumour into the sphenoidal sinus. These temporary aggravations of the symptoms are presumably due to acute degenerative processes, accompanied by swelling of the tumour tissue. It may be said, however, that no histological change in the adenoma has been demonstrable in cases in which tissues have been secured by operation subsequent to periods of radiotherapy.

The experience in the Clinic with radium, so highly recommended by Hirsch, has been far less encouraging. In a number of cases, seeds of radium emanations have been implanted directly in the tumour after its exposure by operation. In other cases radium has been used by intranasal applications without operation. No beneficial results have been seen, and the occasional necrosis of bone resulting from these applications has been a distressing complication. We have had no experience with the extracranial heavily-filtered radium-pack method as advocated by Pancoast.[28]

Medicinal Treatment.—As regards endocrine substitution therapy, we are well-nigh powerless at present. The oral administration of 'whole gland' or of separate pituitary lobe preparations has proved quite valueless in the past. So convincingly true has this been that such treatment of hypophysial disease was abandoned many years ago at this Clinic. However, the recent work of Evans holds out fresh hope in this direction. By intraperitoneal administration of anterior lobe preparations to rats whose hypophysis had been injured, his co-workers were able to overcome the retardation of growth from which the animals suffered. It is possible that some day we may be in possession of endocrine substitution therapy for hypophysial disease quite comparable with that which is available for hypothyroidism, but it appears that it will have to be given in some other way than by mouth.*

Surgical Treatment.—What can we hope to achieve by mechanical measures? In the first place it must be recognized that from the position of the tumour, its intimate relationships to important structures, and its mode of extension around these structures, its complete removal is surgically impossible, even if the attempt were advisable, in the great majority of advanced cases. Moreover, we believe that any operation which aims at

---

* There is at present no justification for calling the administration of pituitrin for diabetes insipidus an endocrine substitution therapy. In fact, the experimental and clinical evidence upon this subject is strongly opposed to such a view. However, until the nature and origin of pituitrin shall have been satisfactorily explained the matter must remain in doubt.

total extirpation is unjustifiable because of the extremely slender chance it has of accomplishing its object and the great hazard with which such an attempt must be associated.

Assuming, then, that the hypophysial adenoma is to be considered incapable of complete extirpation, what can be done for the patient? If the neoplasm is not completely removed, it will certainly continue to grow (though its growth may be retarded by radiotherapy). Furthermore, it will probably continue to produce its noxious secretion if of the eosinophilic variety.

From surgery, therefore, we cannot as yet anticipate any permanent modification of the constitutional symptoms of acromegaly, even though experiences such as we have recorded (cf. *Case* 6) may point in this direction. Much, however, can be done to relieve the distressing consequences of local pressure of the tumour—the headaches and loss of vision; and we would emphasize that it is with this objective alone that the surgery of the hypophysis can be rightly employed.

We are dealing with a tumour which cannot be completely removed, which is enclosed by resistant structures below, and which consequently tends to grow upward and press upon the chiasm, thereby causing blindness. By removing the resistant structures below it, we can not only relieve the tension headaches, but also release the important structures above it from compression. This is one of the main objects of the transphenoidal operation,[29] which produces a decompression from below by removal of the sellar floor and splitting of the dural capsule. We would emphasize that the object of this surgical procedure is not only to remove as much of the tumour as thought safe, but also to relieve the upward pressure of a lesion which cannot be removed entirely, and will inevitably continue to grow, by permitting the growth to enlarge downward. Only the operation from below can accomplish this object. By approaching the tumour from above, it is possible in favourable cases to effect a partial removal and in this way to relieve temporarily the optic fibres from compression. But in the opinion of the Clinic the chief argument against this procedure lies in the fact that incision of the dural capsule, in those cases in which, though bulging, it is still intact, opens the way for a ready intracranial extension of the growth which might otherwise be long postponed.

Admitting the propriety of operating on pituitary adenomata from below, the very great importance of their correct diagnosis becomes evident, for it is particularly dangerous to operate on pituitary lesions other than adenomata by the transphenoidal route. Suprasellar tumours, and likewise the adenomata which have invaded the cranial chamber, must be approached from above, and in this Clinic an osteoplastic transfrontal exposure[30] is greatly preferred to that which approaches the lesion from the side. The transphenoidal operation, as a matter of experience, carries with it very little risk of meningeal infection when conducted in the presence of an adenoma with a ballooned sella.

In the series of 162 cases which have been subjected to operation the mortality has been: in 177 transphenoidal operations, 8·6 per cent; and in 19 transfrontal operations, 5·2 per cent. The transfrontal series is so small

that the figures are scarcely comparable. It is quite probable, nevertheless, that the transphenoidal operation will always have a slightly higher operative mortality than the transfrontal procedure, from the occasional possibility of meningeal infection which it carries with it. However, in dealing with a condition such as pituitary adenoma, an operative mortality of 8·6 per cent does not appear excessive. Even so, it may be said that these inclusive mortality figures are greatly affected by early experiences with advanced lesions and hopeless secondary operations. Since May 1, 1923, a consecutive series of 42 transphenoidal operations has been carried out with but one fatality.

A far more weighty consideration than the difference between an 8·6 per cent and a 5·2 per cent operative mortality is the degree of benefit which is conferred on the majority of the patients by each procedure. The transfrontal operation can hold out little to a patient with an adenoma beyond an exploratory operation with possible temporary relief of pressure symptoms; and there is always the risk of further damage to the chiasm by direct trauma, which defeats the main purpose of the operation. The transphenoidal procedure confers a large measure of relief whose duration is much longer, often extending over many years.

When, therefore, a diagnosis of adenoma can be made with confidence, we believe there is no question that the first surgical step should be a sellar decompression with partial removal of the tumour from below. Later, should definite signs of an intracranial extension persist, the advisability of an intracranial operation for its removal may have to be considered. This is especially to be contemplated when signs of a lateral intracranial extension are present, as evidenced by homonymous hemianopsia, uncinate attacks, etc. Such an extension is less likely to recede into the decompressed sella than is a median one. The transfrontal approach is the more satisfactory in such a case.

We do not consider that the doubtful gain in exposure which Heuer's[31] and Adson's frontolateral operation may offer compensates for the occasional cerebral injuries and much higher mortality-rate with which these procedures have been associated.

To summarize the treatment of hypophysial adenomata, we advocate: A trial of X-ray therapy unless there is imminent danger of loss of vision, when a sellar decompression should be done forthwith. During the course of X-ray treatment the progress of events should be carefully controlled by repeated perimetric examination. If visual impairment becomes greater, a transphenoidal operation should be carried out, with partial removal of the tumour. Later, should symptoms referable to a lateral intracranial extension of the tumour persist, a transfrontal operation should be undertaken. Following all these measures, X-ray treatments should be given in the hope of retarding the further growth of the tumour. They should at first be administered at intervals of three or four weeks, and later the treatments should be adjusted as the progress and circumstances of the particular case demand.

SUMMARY.

1. A clinico-pathological study of 162 examples of pituitary adenomata shows that three fairly definite types of tumour can be histologically recognized and that they represent more or less definite clinical syndromes.

2. The syndrome of acromegaly corresponds with the chromophil adenoma, that of hypopituitarism with a chromophobe adenoma, and the mixed syndrome with a mixed type of adenoma. Case histories are given to illustrate these several syndromes.

3. Though our knowledge of the physiological action of the pars distalis is in its infancy, it may be asserted not only that it exerts an influence on growth, but that the eosinophilic cells are the ones chiefly concerned. In the absence of an increase in the number of these cells, evidences of overgrowth of one sort or another have not been found to occur.

4. We have as yet no knowledge of the biochemical influences which underlie the formation of these adenomata, and can only draw analogies from the better known lesions of the thyroid in arriving at our interpretations of them.

5. The treatment of these lesions is therefore still at the primitive stage in which a radical operative measure, rather than some simpler agent, is called upon to relieve the effects of local pressure on important neighbouring structures.

REFERENCES.

[1] CUSHING, *The Pituitary Body and its Disorders*, 1912. Philadelphia: J. B. Lippincott Co.

[2] BENDA, "Beiträge zur normalen und pathologischen Histologie der menschlichen Hypophysis Cerebri", *Arch. f. Anat. u. Physiol.* (Phys. Abt.), 1900, cccxiv, 373.

[3] LOEWENSTEIN, "Die Entwicklung der Hypophysisadenoma", *Virchow's Arch.*, 1907, clxxxviii, 44.

[4] CUSHING, "The Hypophysis Cerebri: Clinical States of Hyperpituitarism and of Hypopituitarism", *Jour. Amer. Med. Assoc.*, 1909, liii, 249.

[5] MARIE, "Sur deux Cas d'Acromégalie: Hypertrophie singulière non-congénitale des Extrémités supérieures, inférieures, et céphaliques", *Rev. de Méd.*, 1886, vi, 297.

[6] MINKOWSKI, "Ueber einen Fall von Akromegalie", *Berl. klin. Woch.*, 1887, xxiv, 371.

[7] MASSALONGO, "Sull' Acromegalia", *Riforma Med.*, 1892, viii, 74, 87.

[8] BRISSAUD and MEIGE, "Gigantisme et Acromégalie, *Rev. scient.*, 1895, iii, 330.

[9] TAMBURINI, "Contributo allo Pathogenesi dell' Acromegalia", *Riv. sper. di Freniatria*, 1894, xx, 559.

[10] FRÄNKEL, STADELMANN, and BENDA, "Klinische und anatomische Beiträge zur Lehre von der Akromegalie", *Berl. klin. Woch.*, 1900, xxvii, 513, 536, 564.

[11] BABINSKI, "Tumeur du Corps pituitaire sans Acromégalie et avec Arrêt de Développement des Organes génitaux", *Revue neurol.*, 1900, viii, 531.

[12] FRÖHLICH, "Ein Fall von Tumor der Hypophysis Cerebri ohne Akromegalie", *Wien. klin. Rundsch.*, 1901, xv, 883.

[13] BARTELS, "Ueber Plattenepithelgeschwülste der Hypophysegegend (des Infundibulums)", *Zeits. f. Augenheilk.*, 1906, xvi, 530.

[14] PAULESCO, *L'Hypophyse du Cerveau*, 1908. Paris: Vigot Frères.

[15] CROWE, CUSHING, and HOMANS, "Experimental Hypophysectomy", *Johns Hop. Hosp. Bull.*, 1910, xxi, 127.

[16] ASCHNER, "Ueber die Funktion der Hypophyse", *Pflüger's Archiv.*, 1912, cxlvi, 1.

[17] EVANS and LONG, "Characteristic Effects upon Growth, Œstrus, and Ovulation induced by the Intraperitoneal Administration of Fresh Anterior Hypophysial Substance", *Proc. Nat. Acad. of Science*, Baltimore, 1922, viii, 38.

[18] CUSHING, *Dispuitarism* (the Harvey Lecture Series for 1910), p. 31. Philadelphia: J. B. Lippincott Co.
[19] BAILEY and DAVIDOFF, "Concerning the Microscopic Structure of the Hypophysis Cerebri in Acromegaly", *Amer. Jour. Pathol.*, 1925, i, 185.
[20] MCKENZIE and SOSMAN, "The Roentgenological Diagnosis of Craniopharyngeal Pouch Tumors", *Amer. Jour. Roentgen. and Radium Therapy*, 1924, xi, 171.
[21] CUSHING and WALKER, "Chiasmal Lesions, with Especial Reference to Homonymous Hemianopsia with Hypophysial Tumour", *Arch. of Ophthalmol.*, 1918, xlvii, 119.
[22] GOETSCH, CUSHING, and JACOBSON, "Carbohydrate Tolerance and the Posterior Lobe of the Hypophysis Cerebri", *Johns Hop. Hosp. Bull.*, 1911, xxii, 165.
[23] SJÖVALL, "Hypophysis and Hypothalamus", *Acta. Med. Scand.*, 1923, lix, 406.
[24] BAILEY, "Die Funktion der Hypophysis Cerebri", *Ergeb. der Physiol.*, 1922, xx, 163.
[25] SMITH and GRAESER, "Experimental Hypophysectomies in the Rat", *Anat. Record*, 1924, xxvii, 219.
[26] MARTIN and CUSHING, "Primary Gliomas of the Chiasm and Optic Nerves in their Intracranial Portion", *Arch. of Ophthalmol.*, 1923, l, 209.
[27] BÉCLÈRE, "Technique, Résultats, Indications, et Contre-indications de la Roentgenthérapie des Tumeurs hypophysaires", *Revue neurol.*, 1922, xxxviii, 808.
[28] PANCOAST, "Treatment of Brain Tumors by Radium", *Amer. Jour. Roentgenol.*, 1922, N.S. ix, 42.
[29] CUSHING, "Surgical Experiences with Pituitary Disorders", *Jour. Amer. Med. Assoc.*, 1914, lxiii, 1515.
[30] CUSHING, "Les Syndromes hypophysaires au Point de Vue chirurgical", *Revue neurol.*, 1922, xxix, 779.
[31] HEUER, "Surgical Experiences with an Intracranial Approach to Chiasmal Lesions" *Arch. of Surg.*, 1920, i, 368.

RIGHT DUODENAL HERNIA: WITH REPORT OF A CASE SUCCESSFULLY OPERATED ON, THE FOURTH RECORDED RECOVERY.

By FRANCIS R. BROWN, Dundee.

The following is the report of a case of right duodenal hernia. The classification adopted is that given by Moynihan in 1899 in his monograph on retroperitoneal hernia. This very rare condition has also been described as right paraduodenal hernia, and as hernia of the mesentericoparietal fossa of Waldeyer.

The patient, a man of 49 years, was admitted to Dundee Royal Infirmary on Dec. 13, 1922, with the provisional diagnosis of chronic duodenal ulcer. Seven years before he fell from a height, and both bones of the right leg were fractured. At that time he thought he had injured something in his abdomen. He was off work for eighteen months, and 'had never felt the same since'. Three years before admission he underwent an operation for hæmorrhoids. He referred the onset of his present illness to an occasion about two months before admission. While at stool he was 'pressing pretty hard' owing to constipation, and thought he felt something 'go' in the region of the epigastrium. This was followed by pain of a steady, dull, aching character in the epigastrium for one month. He stated that his doctor told him there was a swelling there. (The doctor informed me that only on one occasion did he get the impression of a palpable swelling in the upper abdomen, and as he failed to verify it on subsequent examinations, did not attach any significance to the observation.) The pain, almost constant for a month, gradually became less severe, and latterly had practically disappeared. It had no time relationship to meals, and was neither aggravated nor relieved by taking food. The appetite was good, and there was no vomiting. On examination of the abdomen, nothing definite was made out except slight tenderness on pressure over and just below the xiphisternum. X-ray examination of the alimentary tract was reported to reveal no abnormality.

No definite diagnosis was made, and on Dec. 23, 1922, I performed laparotomy through a high right paramedian incision. On opening the peritoneal cavity no free small intestine was visible, but coils of small intestine were observed 'shining through' a thin layer of peritoneum, exactly as one often sees when dealing with a thin inguinal hernial sac containing unreduced bowel. The first impression received was that there was a second layer of anterior parietal peritoneum. Further investigation showed that the condition was an internal hernia into a large peritoneal sac. The mouth of the sac looked to the left; its posterior boundary was formed by the lumbar vertebræ covered by peritoneum, and in the anterior margin lay the superior mesenteric artery. The rest of the sac, occupying mainly the right half of the

abdomen, was freely movable, and the hand could be passed completely round between it (the sac) and the parietal peritoneum lining the posterior abdominal wall. The contents of the sac were rather more than the upper two-thirds of the small intestine, the jejunum entering the sac about three inches from the duodenojejunal junction, which appeared to be in its normal position. The herniated bowel was easily withdrawn, and was of normal appearance. The first part of the jejunum was free. After reduction of its contents, the greater part of the sac could be brought out of the abdomen,

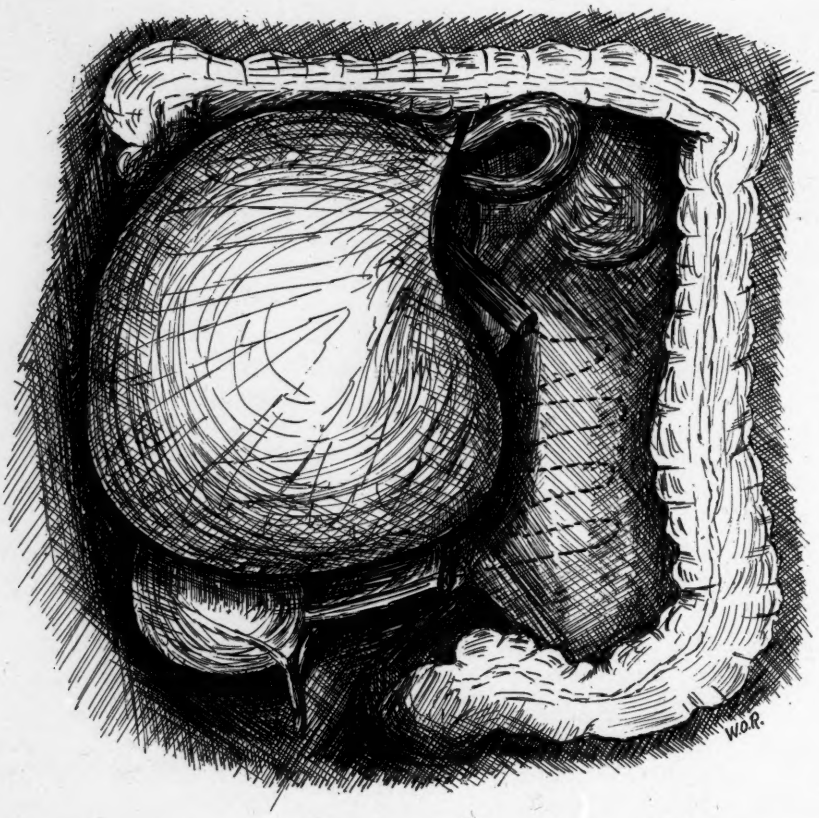


FIG. 250.—*Author's case.* Right duodenal hernia. The orifice of the sac is shown, with afferent jejunum and efferent ileum. Notice the superior mesenteric artery in the anterior margin. The fundus of the sac lies in front of the ascending colon.

and the situation of the orifice, which admitted four fingers, was verified. The sac was turned completely inside out so that the orifice looked to the right, the neck was closed by a catgut suture, and the fundus was removed. (*Figs.* 250–252.) The ascending colon had a definite mesentery, and the cæcum was unduly mobile, which enabled one to remove the appendix easily through the high incision. No other abnormality was observed. The patient made an uneventful recovery, and has had no return of his previous symptoms.

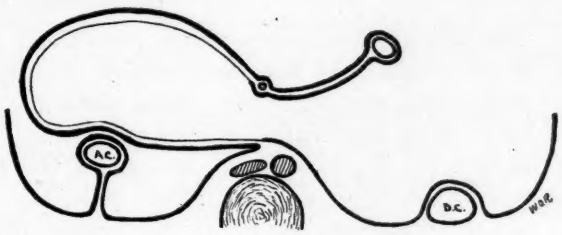


FIG. 251.—*Author's case.* Diagram of transverse section at level of mouth of the sac. Shows the sac lying in front of the ascending colon and mesocolon.

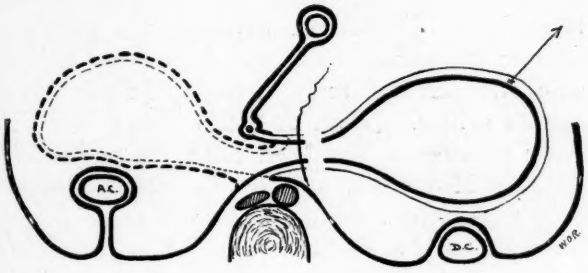


FIG. 252.—*Author's case.* Method of obliteration of sac by eversion and closure of the neck by suture.

FIG. 253. — Diagram of transverse section to show the normal disposition of the mesentery and peritoneum of the posterior abdominal wall—for comparison with *Figs*, 251, 252, 254, and 255.

Fig. 254.* — Sac passing behind the posterior parietal peritoneum. Ascending colon pushed outwards by the hernia when there is no ascending mesocolon.

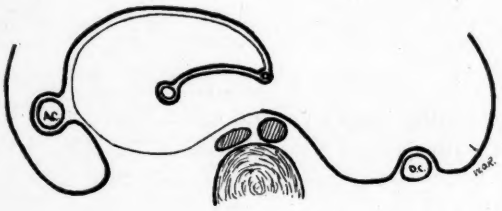
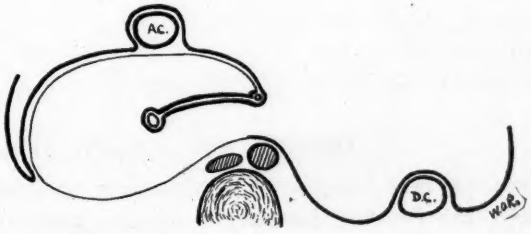


Fig. 255.*—The hernia has burrowed behind the ascending colon, and appears on its outer side. This is the condition commonly found when an ascending mesocolon is present.



* *Figs.* 254 and 255 are diagrams of transverse sections to illustrate the position of the sac in the more usual types of right duodenal hernia.

DISCUSSION.

Moynihan[1] lays down three conditions as invariably present in right duodenal hernia: (1) The sac occupies—at any rate, at first—the right half of the abdominal cavity, lying behind the ascending and transverse mesocolon; (2) The orifice is situated behind and to the left of the sac, on the lumbar vertebræ; (3) In the anterior margin of the sac there lies either the superior mesenteric artery or a continuation of it, the ileocolic artery.

In the case here recorded, the position of the orifice, and the presence of the superior mesenteric artery in the anterior margin of the orifice, are in accord with Moynihan's criteria, but the position of the sac in relation to the posterior parietal peritoneum is unusual. Instead of stripping the posterior parietal peritoneum off the posterior abdominal wall, and burrowing behind the ascending colon and mesocolon, the sac lay freely in front of these structures, being indeed fixed only at its orifice. (*Figs.* 251, 254, 255.)

The presence of an ascending mesocolon has been noted in previously reported cases, e.g., by Broesike, by Moynihan, and by Carson.[2] Gruber[3] reported a case associated with a persistent mesentery for the large bowel, and attached considerable significance to this finding. Nagel,[4] in describing his case, states that "the presence of a persistent mesentery to the ascending colon may have aided in forcing the intestines into the pocket, and it undoubtedly helped to maintain them there".

Abnormalities about the duodenojejunal flexure appear also to be common in this condition. Thus Broesike,[5] in the cases he investigated, found a fusion of the upper few inches of jejunum to the posterior abdominal wall, and believed that this abnormality was essential for the formation of this type of hernia. Moynihan has shown that this condition is not necessary, and that the jejunum may have a free mesentery from its commencement—as in the author's case and others, e.g., Barrs',[6] and Griffith's museum specimen in Leeds Infirmary. On the other hand, the ascending portion of the duodenum may have a free mesentery continuous with the mesojejunum—as found in the cases described by Carson, and Bernardbeig.[7]

Much significance cannot, I think, be attached to the history of hæmorrhoids in this case, although it is conceivable that in some cases there may be pressure on the inferior mesenteric vein, which vessel, Carson states, was present in the posterior margin of the neck of the sac in his case; this feature no doubt caused the enormous dilatation of the veins of the descending colon and sigmoid which he noted. The occurrence of hæmorrhoids in left duodenal hernia (from compression of the inferior mesenteric vein) has been reported (Strazewski[8]), and Moynihan refers to an article by Leichtenstern,[9] who first pointed out the diagnostic significance of this observation.

ORIGIN OF RIGHT DUODENAL HERNIA.

Several somewhat conflicting theories have been brought forward to account for the formation of this type of internal hernia, but as yet it is doubtful if the true explanation is known.

Sir A. Cooper's case of 'mesenteric hernia'—almost certainly of the same nature as the author's—was supposed by him to result from traumatic rupture

of one layer of the mesentery, and the protrusion through the aperture of intestine which would force in front of it the other intact layer as a hernial sac, or from congenital defect in either layer, when a similar effect would ensue.

According to Broesike and Moynihan, right duodenal hernia originates only in the mesentericoparietal fossa, first described by Waldeyer in 1874. Moynihan's description is as follows: "The most usual position of this fossa is in the first part of the mesojejunum, immediately behind the superior mesenteric artery and immediately below the duodenum. The fossa varies considerably in size. The fossa has its orifice looking to the left, its blind extremity to the right and downward. In front it is bounded by the superior mesenteric artery, and behind by the lumbar vertebræ. The peritoneum of the left leaf of the mesentery lines the fossa; that of the right covers the blind end, and is then continued directly into the posterior parietal peritoneum. A forcible enlargement of the fossa would thus result in a tearing up of this layer of peritoneum lining the posterior abdominal wall".

Klob,[10] the first to describe this condition accurately, and later, Jonnesco,[11] believed the hernia to originate in the inferior duodenal fossa. More recently, Nagel writes: "While the majority of right duodenal hernias probably arise in the fossa of Waldeyer, it is reasonable to assume that some of them may originate in the inferior duodenal fossa when situated very low, near the beginning of the third portion of the duodenum and over the center of the vertebral column, or even to the right of the middle line". The usual position of the inferior fossa is high and to the left of the middle line. This low position was found in four of the bodies examined by Nagel. "Herniation into such a fossa", he writes, "would naturally progress toward the right, and by a peeling back of its superior peritoneal margin, until it reached the mesenteric vessels, would form a typical right paraduodenal hernia".

Edmund Andrews[12] advances an embryological explanation of the causation of duodenal hernia, which term he considers a misnomer. He believes that the condition is "a congenital anomaly due to imprisonment of the small intestine beneath the mesentery of the developing colon". He characterizes as absurd and grotesque the prevalent conception that these enormous hernias originate in small peritoneal pouches, and grow in size by gradual expansion of the sac. In support of his contention, he states: (1) Differential pressure within the abdomen is utterly lacking, so that any *vis a tergo* to account for the formation or growth of such hernia is totally absent. (2) There are literally hundreds of similar folds and fossæ in the peritoneum, many of which are of much greater size, and they are practically never the sites of such 'hernias'. (3) In all but a very small minority of cases reported, the degree of herniation has been total or subtotal. (4) A case of total hernia in a new born infant has been reported (left duodenal hernia—Vogt). Andrews writes "Surely one cannot believe that intra-abdominal pressure in utero has been the cause of such a 'hernia'". (5) The herniated viscera are never anything but small bowel. The presence of omentum in the sac has never been reported. In only one case, that of Pybus (left duodenal hernia), was a few inches of the descending colon herniated. (6) In many of the cases there has been an almost universal growing together of the contents of the sac. This

condition, termed 'totalis accreta' by Kohlman, was present in Andrews' case, and he considers the adhesions to be derived from retroperitoneal tissue rather than the result of inflammation. Andrews explains production of right duodenal hernia as follows: "Suppose that the rotation of the umbilical loop is not carried to completion. The cæcum then would not lie superior to the small intestines" (Andrews illustrates it lying at a lower level on the left side of the abdomen), "and as it grew to the right, the small bowel would be caught in its mesentery, and finally, when its mesentery became adherent to the right posterior abdominal wall, its imprisonment would be complete. The superior mesenteric and ileocolic artery would lie in the free edge of the sac. All the conditions of a right duodenal hernia are exactly reproduced". He explains the formation of left duodenal hernia as "merely a higher degree of the same process", and believes that cases of mesocolic hernia and pericæcal hernia may have a similar origin.

Against Andrews' theory, at first sight a plausible explanation, can be made the following criticism. Normally, during the second stage of rotation of the mid-gut loop at the tenth week, the small intestines pass to the left side of the abdomen behind the superior mesenteric vessels; the cæcum then passing to the right side and eventually descending to the right loin as the colon elongates; the ultimate result of this rotation being an anti-clockwise turn of 270° about the axis of the superior mesenteric artery (Dott).[13] When this rotation does not occur, the small intestines occupy the right hypochondriac, lumbar, and iliac regions. The colon is confined to the left side. The small intestine, so situated, would not only effectively prevent the ascending colon and mesocolon from reaching and adhering to the right posterior abdominal wall, but, instead, would tend to perpetuate the left-sided position of the ascending colon, which would thus lie alongside the descending colon. Many cases of this type of non-rotation have been reported, the chief surgical interest being left-sided appendicitis.

In the author's case, the hernial sac lay, as already emphasized, freely in front of the ascending colon and mesocolon, a position which is inconsistent with Andrews' embryological explanation.

SUMMARY OF RECORDED CASES OF RIGHT DUODENAL HERNIA.

Nagel collected and summarized 29 cases, including his own; of these, 17 were noted by Moynihan[1] in 1906. Rendle Short,[14] in his paper on retroperitoneal hernia, confines himself to those cases producing symptoms during life and in which an operation was performed. To Nagel's list of such cases, he added that of Novak and Sussmann,[15] a man, age 34, who recovered—making thus a total of 3 recoveries and 10 deaths. Two more authentic cases are now added to the list: Bernardbeig's, a man of 56, operated on unsuccessfully for acute obstruction in November, 1924; and the author's, operated on in December, 1922, and now recorded.

Levin and Ellis[16] reported a case of hernia into the inferior duodenal fossa in a boy of 8 years who recovered after operation. Levin considers it to be a right duodenal hernia. At operation about 15 to 18 in. of the commencement of the jejunum were found in a sac in the mesentery to the right

of the vertebral column. The mouth of the sac looked upwards and to the left, and was in the situation of the inferior duodenal fossa. The superior mesenteric artery was not identified, and Levin states: "In this particular case, I am quite certain that there was no vessel in the anterior boundary of the neck, for after I had made my incision over the 'tumour' I slipped my finger into the constricting ring and cut through it: there was no bleeding, therefore there could not have been a vessel of any size in the neck". This case appears to be similar to Molin's hernia into the inferior duodenal fossa, and cannot, I consider, be accepted as a right duodenal hernia.

Table I (*after Nagel*).—Recorded Cases of Right Duodenal Hernia. (Authentic Cases.)

	Observer	Year	Age	Sex	When Diagnosed	Symptoms of Acute Obstruction	Operation	Result
1	Klob	1861	36	M.	At necropsy	—	No	—
2	Gruber	1868	25	M.	At necropsy	—	No	—
3	Moutard-Martin ..	1870	—	—	At dissection	—	No	—
4	Guy's Museum specimen ..	1870 1871	—	—	Museum specimen	No	No	—
5	Fürst	1884	61	M.	At necropsy	—	No	—
6	Zwaardemaker ..	1884	Adult	M.	At necropsy	Yes	No	—
7	Quénu (Jonnesco)	1885	50	M.	At operation	Yes	Yes	Death
8	Gerard-Marchant..	1885	—	—	At dissection	—	No	—
9	Broesike	1884 1885	2	M.	At dissection	—	No	—
10	Broesike	1886	Adult	M.	At dissection	—	No	—
11	Barrs	1891	18	M.	At necropsy	Yes	No	—
12	Clarke	1893	Adult	M.	At operation	Yes	Yes	Death
13	Rose	1895	68	F.	At operation	Yes	Yes	Death
14	Morestin	1896	Adult	M.	At dissection	Yes	No	—
15	Neumann	1898	55	F.	At operation	Yes	Yes	Cure
16	Griffith (Moynihan)	1898	—	—	Museum specimen	—	No	—
17	Kuppers	1899	—	—	—	—	—	—
18	Schwalbe	1903	14 months	M.	At dissection	—	No	—
19	Schwalbe	1903	Adult	M.	At dissection	—	No	—
20	Selby	1904	40	M.	At operation	Yes	Yes	Death
21	Paton	1906	3 months	—	At operation	Yes	Yes	Death
22	Haasler	1907	43	F.	At necropsy	—	Yes	Death
23	Haasler	1907	10	M.	At operation	Yes	Yes	Death
24	MacCullum and Miller	1908	41	M.	At operation	Yes	Yes	Death
25	Van Rossum ..	1909	—	—	—	—	—	—
26	Merrigan	1911	—	—	At dissection	—	—	—
27	Mueller	1911	47	M.	At operation	Yes	Yes	Death
28	Carson	1912	29	M.	At operation	Yes	Yes	Cure
29	Nagel	1923	55	M.	At necropsy	No	Yes	Death
30	Novak and Sussmann ..	1924	34	M.	At operation	Yes	Yes	Cure
31	Bernardbeig ..	1925	56	M.	At operation	Yes	Yes	Death
32	Brown	1925	49	M.	At operation	Chronic	Yes	Cure

Table I is a summary of the 32 authentic cases, including my own, in the literature. Of these, 15 were operated on; 15 had symptoms of acute

obstruction, and 3 of these died without operation having been performed. In 2 cases (Nagel's and one of Haasler's), although laparotomy had been performed for other conditions, the presence of right duodenal hernia, found at necropsy, was unsuspected during life, and it apparently had given rise to no symptoms. Thus 13 cases were operated on because of symptoms produced by the hernia, and there were 4 recoveries.

CLINICAL FEATURES AND DIAGNOSIS.

So far, not a single case of right duodenal hernia has been diagnosed before operation or necropsy.

It may be observed at any age. The youngest patient was that of Paton, age 3 months; the oldest, reported by Rose, was a woman of 68 years. In the male sex 21 cases occurred, and 3 in females; in 8 cases the sex is not noted.

The great majority were operated on for symptoms of acute obstruction, which may follow several similar attacks or suddenly occur in an apparently previously healthy patient. In the more chronic type the symptoms have been likened to those of chronic duodenal ulcer, but they resemble rather those of chronic duodenal ileus. In others there may be more or less severe persistent pain with little or no vomiting, as in chronic obstruction. Lastly, the condition may remain symptomless, and be found at necropsy. The most important physical signs are:—

1. *Vomiting.*—This may be absent or scanty even when obstruction is complete. If continued, the vomitus will consist mainly of bile: there can be no regurgitation of small intestine contents. In Carson's case constant vomiting of bright-green material was a feature.

2. *Visible Peristalsis.*—A sign of chronic obstruction occurring in the bowel above the site of constriction. In Carson's case, and in that of Levin and Ellis, peristaltic waves passing from left to right across the epigastrium were observed. In both these cases, subsequent operation showed dilatation of the stomach and duodenum. While marked peristaltic waves of the herniated intestine may occur if the efferent loop is obstructed, it is doubtful if such peristalsis would be visible except in a very thin patient, owing to the deep position of the hernia behind the ascending colon and mesocolon—the most common situation.

3. *Palpable Swelling.*—This, the most important diagnostic sign when present, is described by Moynihan as "a *palpable, definite, resonant mass* which lies at first to the right and lower part of the abdomen, but spreads finally over almost the whole abdominal cavity. The tumour may bear a very obvious relation to the clinical condition of the patient, becoming more tense and prominent and very much more tender when the symptoms undergo exacerbation. As the symptoms decline in severity, the tumour becomes less aggressive. On auscultation, distinct, gurgling sounds may be heard anywhere in the tumour". In Carson's case the percussion note over the tumour was dull, and at operation the small intestine was withdrawn in a collapsed condition from the sac, which of course would explain the lack of resonance on percussion.

4. *Result of X-ray Examination.*—(*a*) Where there is no obstruction. In Nagel's case X-ray examination carried out two months before death showed the colon filling the left half of the abdomen, with coils of small intestine grouped to the right. This appearance was considered to represent incomplete intestinal rotation, and no further significance was attached to it. (*b*) Where there is chronic obstruction of the afferent loop, the X-ray picture will be similar to that found in chronic duodenal ileus—namely, dilatation of the stomach and duodenum with delay in emptying.

5. *Toxæmia and Collapse.*—These will be intense in acute obstruction if and when practically the whole of the small intestine is strangulated.

TREATMENT.

As long ago as 1906, Moynihan wrote: "In a certain proportion of cases it is likely in the future that an operation will be undertaken after a correct diagnosis has been made". While in a few cases of left duodenal hernia the condition was clinically diagnosed, there is still, as already mentioned, no similar record amongst those of the right variety.

Obstruction, when present, may be due to: (1) Constriction of the intestine by the orifice, although in most cases this is fortunately so large that strangulation does not occur. (2) Adhesions about the orifice of the sac. Thus Bernardbeig states that in his case the orifice was reduced in size by adhesions, which were broken down during the operation, and which played a very important part in the strangulation. (3) Axial twisting or volvulus of the intestine at the neck of the sac, as reported by several writers (Neumann, Carson, Bernardbeig, and others). The author suggests that obstruction may also occur outside the sac, and affect the bowel proximal to the orifice. The weight of the herniated intestine in its dependent sac will so drag on the root of the mesentery that constriction of the third part of the duodenum by the cord-like superior mesenteric artery is likely to result. This would give rise to the condition of duodenal ileus. In such an event, there would be no sudden increase in size of the 'tumour', since the efferent loop is not necessarily constricted.

Reduction, by traction on the afferent or efferent loop of intestine, is generally easy, and spontaneously relieves the obstruction, however caused. Should the orifice have to be enlarged, wounding of the superior mesenteric artery must be carefully avoided. The inferior margin only of the orifice may be incised.

If distention of the strangulated gut prevents reduction, the sac should be entered through an avascular space to the right of the superior mesenteric artery, and the bowel withdrawn, opened, and emptied, after which reduction through the orifice should be easily accomplished.

After reduction, closure of the neck of the sac should be attempted, if the condition of the patient permits, in order to prevent the possibility of recurrence. In at least two cases (Paton's and Mueller's), where this procedure was not carried out, it was found at post-mortem examination that a considerable quantity of gut had re-entered the sacs.

Partial obliteration of the neck of the sac by suture was performed in

two of the previously reported successful cases (Neumann, and Novak and Sussmann). In Carson's no attempt was made to close the opening. In the author's case the disposition of the sac rendered eversion, and closure of the neck, a comparatively simple procedure.

For the figures illustrating this article, I am indebted to Mr. W. O. Reid, Dundee.

REFERENCES.

[1] MOYNIHAN, Sir BERKELEY, *Retroperitoneal Hernia*, 2nd ed., 1906.
[2] CARSON, *Proc. Roy. Soc. Med.* (*Surg. Sect.*), 1912, v, 214.
[3] GRUBER, *Arch. f. path. Anat., etc.*, Berlin.
[4] NAGEL, *Collected Papers of the Mayo Clinic*, 1923, xv, 135.
[5] BROESIKE, *Ueber intra-abdom. Hernien und Bauchfelltaschen*, Berlin, 1891.
[6] BARRS, *Lancet*, 1891, Aug.
[7] BERNARDBEIG, *Bull. et Mém. Soc. nat. de Chir.*, 1925, March 14, 284.
[8] STRAZEWSKI, "Médecine russe", *Jour. hebdom. de Méd. et d'Hygiene*, 1888.
[9] LICHTENSTERN, *Ziemmsen's Cyclopœdia.*
[10] KLOB, "Hernia Retroperitonealis", *Woch. d. Zeits. d. K. K. Gesellschaft d. Aertze in Wien*, 1861, June 12, No. 24.
[11] JONNESCO, *Hernies internes rétropéritoneales*, Steinheil, Paris, 1890.
[12] ANDREWS, EDMUND, "Duodenal Hernia: a Misnomer", *Surg. Gynecol. and Obst.*, 1923, Dec., xxxvii, 740.
[13] DOTT, NORMAN M., "Anomalies of Intestinal Rotation," *Brit. Jour. Surg.*, 1923, Oct., xi, 251.
[14] SHORT, A. RENDLE, "Retroperitoneal Hernia", *Brit. Jour. Surg.*, 1925, Jan., xii, 45.
[15] NOVAK and SUSSMANN, *Jour. Amer. Med. Assoc.*, 1924, May, 1664.
[16] LEVIN, J. J., and ELLIS, L. E., *Brit. Med. Jour.*, 1924, ii, 98.

SOME UNUSUAL MANIFESTATIONS OF SPREAD BY IMPLANTATION OF PAPILLOMATA OF THE URINARY TRACT.

By B. C. MAYBURY, London, and S. C. DYKE, Wolverhampton.

Few types of new growth exemplify better the process of spread by direct implantation than the papillomata of the urinary tract. The facility with which, by the spontaneous dissemination of seedlets, those of the bladder spread over the mucous membrane of that organ is one of their best recognized characteristics, and their recurrence as the result of accidental implantation in operation wounds in the vesical wall is not rare. The two cases described below are reported with the view of drawing attention to some less common manifestations of this power of spread by implantation. A further point of very great interest in both cases is the rapid growth of secondary tumours after the removal of the primary ones. In view of the fact recently demonstrated by Murray,[1] that the presence of a primary cancerous tumour exercises an inhibitory effect upon the growth of implants of tumours of a similar type, it would appear that something more than coincidence was concerned in this phenomenon. In the first case the original tumour, though histologically of exactly the same type as a vesical papilloma, occurred in the renal pelvis, upon the epithelial lining of which structure implantation and growth of the seedlets occurred. In the second case implantation and growth of seedlets from a vesical papilloma took place altogether outside the urinary tract in the tissues of the abdominal wall; the recurrences, three in number, were remarkable in that, while the first, like the primary growth, was histologically simple, the succeeding recurrences showed a progressive change towards malignancy.

The first case was that of a male, age 45, with a history of repeated attacks of hæmaturia extending over a period of six years. As a rule the bleeding was unaccompanied by pain, but severe left-sided renal colic occurred during the first attack. One bout of hæmaturia, which lasted a month, followed on the patient's being thrown out of a car; but with this single exception he could assign no cause for the attacks. For the last twelve months the hæmaturia had been constant, the patient never having passed a clear specimen. The urine had been examined for organisms more than once, but cultures had invariably proved sterile, and no tubercle bacilli had been found.

When first seen the patient was somewhat thin, but not very anæmic, in spite of the prolonged and continuous loss of blood. Clinical examination revealed nothing abnormal; neither kidney could be palpated. Skiagrams showed no abnormal shadows. The urine was of a port-wine colour, acid, and

contained protein; microscopically there were many epithelial cells and large numbers of red and pus cells, the two latter being present in approximately equal numbers; no casts were seen; cultures were sterile and no tubercle bacilli were found. Cystoscopic examination under an anæsthetic showed that the blood was coming from the left ureter, the jets from the right being normal and becoming coloured with indigocarmine in seven minutes. The bladder itself was normal. A diagnosis of papilloma of the pelvis of the kidney was made, and, after a second cystoscopic examination to confirm the previous

FIG. 256.—Mesial section of kidney removed from *Case* 1.

findings, nephrectomy was performed by the loin route on the left side. The patient made an uninterrupted recovery from the operation.

The kidney, half of which is shown in ***Fig.* 256**, is considerably enlarged. Growing from the pelvis, and partly obstructing the lumen, is a large papilloma which has caused dilatation of the calices. Secondary seedlets of smaller size and presumably younger can be seen in other parts of the hydronephrotic sac, and a group quite separate from the primary tumour is present in one of the lower calices.

Examination, both of the large papilloma at the outlet of the pelvis and also of other smaller ones taken at random from elsewhere in the wall of the hydronephrotic sac, shows them all to be of exactly the same type. They consist of a filiform and branching connective-tissue core containing well-formed blood-vessels, covered with many layers of epithelium of transitional type (*Fig.* 257). The histological appearances are exactly similar to those of an ordinary papilloma of the bladder. The epithelial cells, both in their individual appearance and their general arrangement, conform closely to the

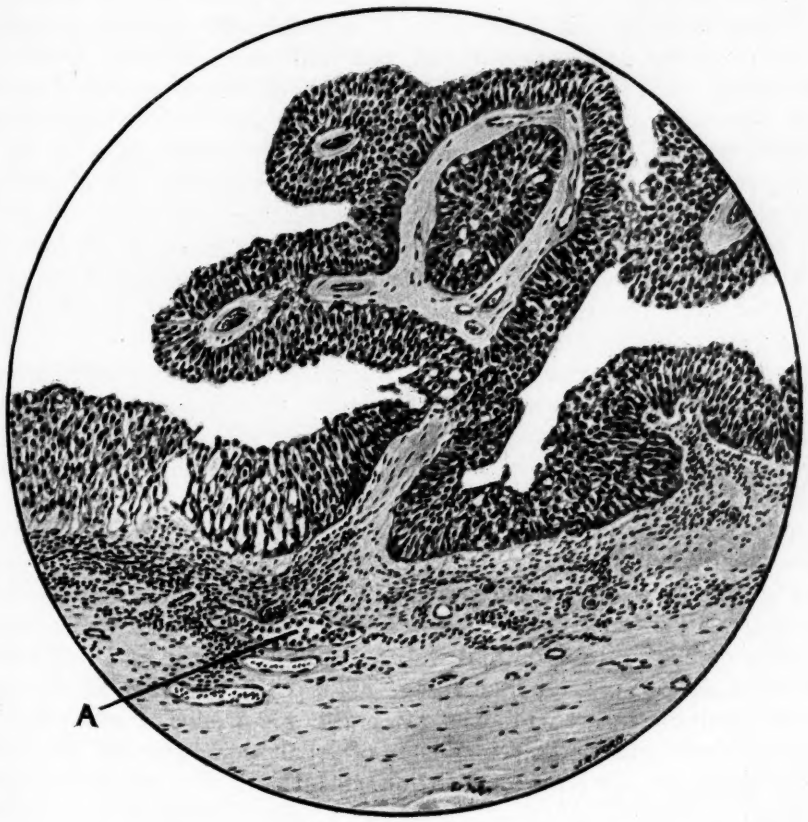


FIG. 257.—Microscopical appearance of the papilloma of the pelvis of the kidney shown in *Fig.* 256. The tumour is similar to an ordinary papilloma of the bladder. There is no evidence of invasion by the epithelial cells. Note the polymorphs present in the vessel at A.

transitional type. A portion of the pelvic wall was included in each piece of tissue sectioned, but in no instance was any indication of invasion by the epithelial growth to be seen. On this evidence, and on the typical nature of the tumours, the papillomata were deemed, in spite of their spread by dissemination, to be benign.

The pelvic wall was greatly thickened by fibrosis, and showed considerable infiltration by inflammatory cells of the plasma-cell type beneath the mucous membrane. No polymorphs were present in these collections of inflammatory

cells, but many of the smaller vessels in the subepithelial tissue were filled with them. The pelvic epithelium between the papillomatous growths was thickened, and consisted of more layers than normal.

The presence of pus cells in the urine in such large numbers as to cast some doubt upon the provisional diagnosis is a point of some interest in this case. Their occurrence in infinitely greater numbers than could be accounted for by the amount of blood present suggested the presence of an infective condition in the kidney, which, however, the results of culture of the urine and subsequent microscopical examination of the kidney proved not to be the case. In the description of the histological appearances of the tumour given above, it was pointed out that signs of a mild and chronic inflammatory process were present in the pelvic wall, but that polymorphs were not among the infiltrating cells. Attention was, however, drawn to the fact that such cells had collected in large numbers in the smaller vessels; a vessel containing such polymorphs is shown at **A** in *Fig.* 257. This stagnation of the polymorphs in the smaller vessels has long been recognized as one of the earliest manifestations of an inflammatory process and as preceding their actual passage by diapedesis from the vessels. It is the blood from the smaller superficial vessels which passes into the urine in cases of papillomata of the urinary tract, and the stagnation of the polymorphs in these vessels would seem to account for their excess in the blood thus passed.

Nine months after the operation, the patient returned with a month's history of recurrence of hæmaturia of exactly the same type as previously experienced. He looked ill and had lost a considerable amount of weight. On examination, the right kidney was found to be enlarged and hard but movable. A provisional diagnosis of papilloma of the remaining kidney was made, but in view of the serious condition of the patient and the impossibility of further operative treatment no cystoscopic examination was undertaken.

The renal swelling increased rapidly in size and later became fixed; from it there extended a large, hard, finely nodular plaque, which was adherent to the anterior and lateral abdominal wall and finally reached to well below the level of the anterior superior iliac spine. The patient became more and more emaciated, and died three months after the recurrence of the hæmaturia. Throughout there was neither any sign of local recurrence on the left side, nor apart from the extreme emaciation was there any clinical evidence of metastases.

Unfortunately there was no autopsy, but there can be little doubt but that the tumour on the right side arose in the kidney and was malignant in nature; probably it commenced as a papilloma similar to the growth removed with the left kidney.

It is conceivable that the removal of the papilloma with the left kidney had the effect of withdrawing the inhibitory effect of this primary tumour upon an existing similar tumour in the right kidney and thus enabled the latter to grow and later become malignant in nature.

In the second case, the patient, a female, 57 years of age, was admitted to St. Thomas's Hospital on Oct. 1, 1923, with a six months' history of attacks of painless hæmaturia. Physical examination was negative. The

urine was acid and contained red and pus cells. Cystoscopic examination demonstrated a moderate-sized, pedunculated papilloma free from phosphatic deposit growing from the trigone below and obscuring the right ureteric orifice. On Nov. 7 the tumour was removed through a long suprapubic incision. It was found to be of the ordinary villous type, about the size of an almond, and attached by a fairly narrow pedicle to the vesical wall, a portion of which was excised with it. The resulting raw area was obliterated by approximating the cut edges of the vesical wall with catgut sutures. The suprapubic wound was closed, and a drain inserted down to the suture line in the bladder. A urinary fistula formed, but healed in a month. On Jan. 1, 1924, cystoscopy showed the vesical scars quite sound and no sign of recurrence. The patient was discharged a few days later.

The specimen as submitted for microscopy consisted of a small portion of the bladder wall about 1·5 cm. long, on which was growing a villous papilloma. Microscopically the tumour showed the ordinary transitional type of epithelium; mitoses were not particularly in evidence, and both the appearance and general arrangement of the cells were quite typical. The base of the papilloma showed no tendency to invade the wall of the bladder, and it was passed without hesitation as benign, so far as morphological criteria avail in making a decision.

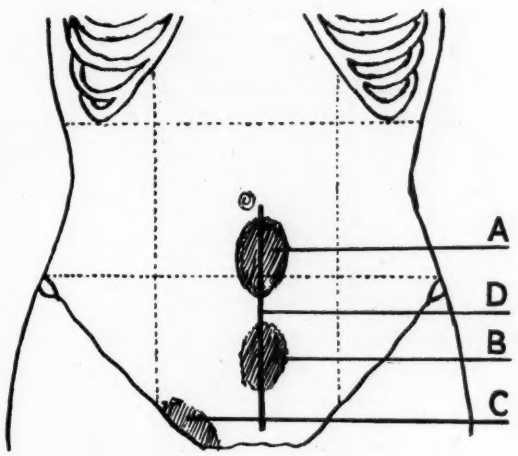


FIG. 258.—Diagram showing the approximate sites of 'graft-recurrences' in the abdominal wall after the suprapubic removal of a simple vesical papilloma (*Case* 2). A indicates the site of the first, B the second, and C the third recurrence, respectively. The suprapubic scar of the original operation is indicated at D.

On May 7, 1924, six months after the original operation, the patient was readmitted complaining of a gradually increasing painful swelling of three months' duration in the suprapubic scar. She had had no recurrence of hæmaturia. On examination there was a fairly well-defined, firm, oval, tender tumour about the size of a hen's egg, situated in the abdominal wall immediately beneath and adherent to the upper part of the suprapubic scar. The approximate site of the tumour is shown in *Fig.* 258, A. The skin overlying it was inflamed, and fluctuation was present in the centre. On the supposition that the swelling was an abscess, it was incised on May 10, but only blood-stained fluid and some friable 'granulation tissue' were evacuated. On May 19 the tumour was widely excised, portions of both rectus muscles and their sheaths being removed with it; the peritoneal cavity was not opened. Some difficulty was experienced in closing the wide gap in the abdominal wall. The bladder was examined with the cystoscope and was found free from recurrence. The patient made an uninterrupted recovery, and was discharged on June 23.

The tumour is shown in cross-section in *Fig.* 259. At the top of the specimen can be seen the skin of the abdominal wall with the upper part of the healed scar. The tumour itself is cut across, and is represented by a ring of white in the centre of which is a red mass of blood-clot. A very well-marked layer of fibrous tissue sharply limits its periphery from the surrounding structures. A portion of the specimen, including both the central tumour mass and the surrounding fibrous tissue, was removed for microscopy. The histological appearances are shown in *Fig.* 260. The central mass consists of epithelial cells of transitional type, together with a certain amount of fibrous stroma. The relation of these two elements to each other shows quite clearly that the stroma represents the central connective-tissue core of the papilloma upon which the epithelial cells are applied. In appearance and arrangement the epithelial cells conform absolutely to type; their only departure from the strict normal is in the presence of numerous mitoses. As shown in *Fig.* 260, the margin of the epithelial cell masses is for the most part sharply defined where it meets the surrounding reactionary fibrous tissue. In one or two places, indeed, there does appear a tendency for processes of the epithelial cells to pass out into this fibrous barrier, which shows a fairly intense infiltration by mononuclear inflammatory cells.

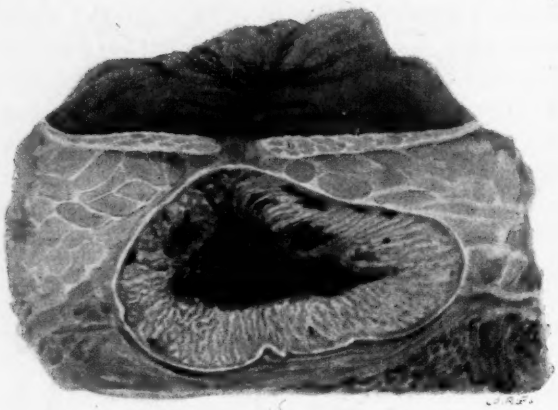


FIG. 259.—Half of the first tumour removed from the abdominal wall in *Case* 2. The skin, together with a portion of the healed scar, is seen at the top of the specimen. The cross-section shows the tumour as a ring of white, and in the centre a mass of red blood-clot. A very well-marked layer of fibrous tissue sharply limits the periphery. A portion of the left rectus muscle is seen at the bottom right-hand corner.

These last facts, together with the frequency of mitosis noted above, were regarded as suspicious; but on consideration of the very typical nature of the tumour as a whole and its wide removal, a favourable prognosis was given so far as recurrence was concerned.

On Aug. 13 the patient was re-admitted with a history of the recurrence of a small painful tumour in the lower part of the suprapubic scar shortly after she had left hospital; this had gradually increased in size and finally broken through the skin, since when it had continuously discharged a blood-stained fluid. On examination there was a swelling similar to the previous recurrence occupying a corresponding position deep to the lowest part of the suprapubic scar (*Fig.* 258, B); it was, however, somewhat smaller, rather firmer, and slightly less defined; there was no fluctuation. In the centre of the tumour there was a sinus surrounded by a prominent mass of reddish-blue granulation tissue partly covered by a thin layer of epithelium. From the sinus was discharged a certain amount of blood-stained fluid. On Aug. 16 the tumour was freely excised with about three-quarters of an inch of the surrounding healthy tissue; small portions of the parietal peritoneum and

bladder were included; the latter appeared normal, and was not attached to the tumour. The opportunity was taken of inspecting the inside of the bladder, and no sign of recurrence was seen. The cut edges of the various layers of the abdominal wall could not be approximated completely, but the wound was closed by suturing the skin under considerable tension.

The tumour is shown in cross-section in *Fig.* 261 and is somewhat similar to the previous specimen. The most striking difference, however, is the absence of any definition of the periphery of the growth, it being impossible

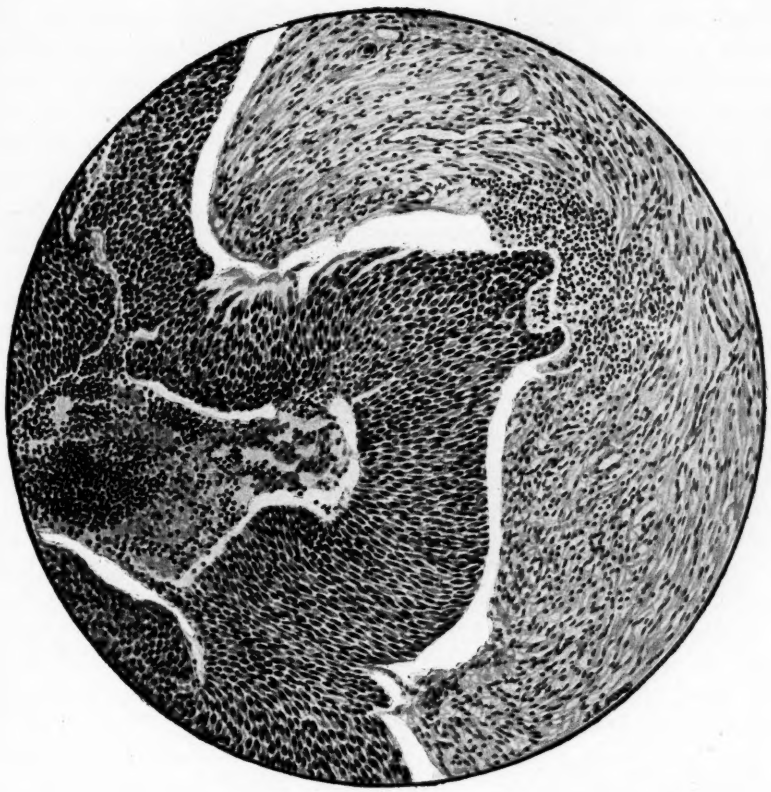


FIG. 260.—Microscopical section of the tumour shown in *Fig.* 259. The epithelial cells, of uniform size and shape, are arranged in masses upon a connective-tissue core. There is no definite invasion, although in one or two places there does appear a tendency for the epithelial processes to pass into the surrounding barrier of fibrous tissue.

in many places to see where the growth ends and the normal tissues begin. The extension of the tumour can be traced to the skin, where it forms a small cauliflower excrescence.

Microscopical examination showed this second recurrence to consist of transitional epithelial cells of the same type as seen in the first recurrence, but now of undoubted malignancy. As shown in *Fig.* 262, the typical arrangement around a central connective-tissue core has been lost, and the cells are disposed irregularly in relation to each other; the characteristic size and

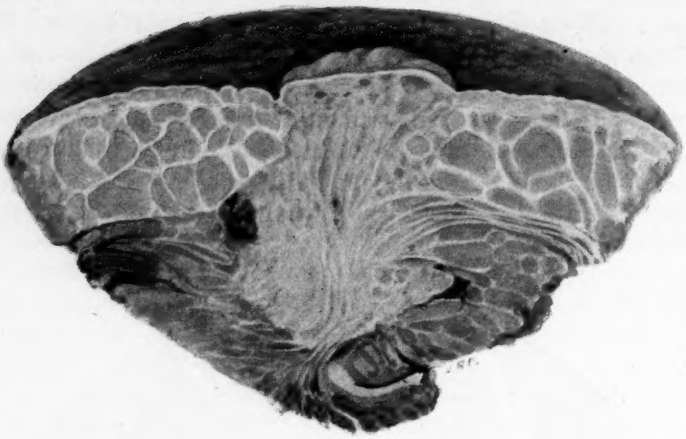


FIG. 261.—Half of the second tumour removed from the abdominal wall in *Case* 2. Contrast with *Fig.* 259. Note the absence of any definition of the periphery of the growth. The extension of the tumour can be traced to the skin, where it forms a small excrescence.

FIG. 262.—Microscopical section of the tumour shown in *Fig.* 261. Contrast with *Fig.* 260. The epithelial cells, of different sizes and shapes, are arranged in irregular masses, which are invading the surrounding fibrous tissue.

shape of the cells has largely disappeared. Finally, as shown in the illustration, the epithelial masses are clearly invading the surrounding fibrous tissue. Mitotic figures are of frequent occurrence in the epithelial cells; curiously enough, however, although all the other features, both histological and clinical, point to this recurrence as being of a much more malignant type than the preceding one, the actual number of dividing cells present in an equal number of fields is considerably less than in the first recurrence.

On Sept. 11, while the patient was still in hospital, a third recurrence was noticed deep to the muscles of the abdominal wall, firmly adherent to the inner portion of the right horizontal ramus of the pubes (*Fig.* 258, C). In view of the histological findings of the last tumour removed, and the fixation of the present one, further operative interference was considered useless.

The first recurrence of this tumour in the abdominal wound undoubtedly occurred as the result of implantation of seedlets from the original papilloma into the operation wound in the course of its removal. The fact that all three recurrences appeared at quite different sites in the abdominal wound, and the wide removal of the first two, preclude the possibility of the later recurrences having arisen from portions of their predecessors left behind at operation. There can be little doubt that all three recurrences arose from seedlets sown into the wound at the original operation.

SUMMARY.

Two cases illustrating unusual manifestations of the power of spread by implantation possessed by papillomata of the urinary tract are reported.

In the first case the original papilloma occurred in the renal pelvis, and implantation took place on the walls of the resulting hydronephrosis. Removal of the affected kidney together with the tumour was followed by the rapid growth of a malignant tumour in the remaining kidney. The urine in this case showed much pus in the absence of any infective process; an explanation is offered of this phenomenon.

In the second case, after removal of a simple vesical papilloma, three 'graft-recurrences' occurred in three separate places in the tissues of the abdominal wall, each appearing shortly after the removal of the previous one; it is suggested that all three arose from portions of the original tumour accidentally implanted at the first operation. The primary tumour was histologically non-malignant, but the successive recurrences showed a steady progress towards malignancy.

It is suggested that the course of these cases offers an illustration of the inhibitory effect exercised by the presence of a primary tumour in the tissues upon the rate of growth of secondaries and their degree of malignancy.

Our thanks are due to Sir Cuthbert Wallace for permission to publish the notes of the second case.

REFERENCE.

[1] MURRAY, J. A., *Eighth Scientific Report of the Imperial Cancer Research Fund*, 1923.

SHORT NOTES OF RARE OR OBSCURE CASES

STRANGULATED FEMORAL HERNIA ASSOCIATED WITH AN APPENDIX ABSCESS IN THE HERNIAL SAC.

By NORMAN HODGSON, Newcastle-upon-Tyne.

The following case is of interest on account of the rare association of the two conditions and of the difficulty in diagnosis.

The patient, a woman, age 70, was admitted to hospital with intestinal obstruction of four days' duration. There was definite visible peristalsis of the small intestine. In the right femoral region there was a swelling the size of a walnut, with an active sinus on its inner side. There were no other physical signs. The patient stated that following an attack of abdominal pain eight months previously, this swelling appeared and burst, discharging pus; then it healed rapidly. She had had several mild attacks of abdominal pain, also recurrence of the abscess, but had not associated the two conditions. Since the first attack she had never felt well and had for the most part been confined to bed.

The diagnosis made was intestinal obstruction, probably due to a carcinoma of the colon, the swelling in the groin being thought to be a suppurating lymphatic gland.

Under general anæsthesia an incision was made into the swelling and a small quantity of pus evacuated. The abdomen was then explored through a median subumbilical incision. Collapsed small intestine presented, and following this down, it led into the femoral canal on the right side. Gentle traction delivered a knuckle of strangulated small intestine which quickly recovered its normal appearance. On inspecting the femoral ring, the appendix was seen running into the canal. It was firmly adherent to the posterior wall of the canal and was separated with difficulty. The appendix was removed and the stump buried. The abdomen was closed without drainage. The incision in the groin, which communicated with the hernial sac, was packed with gauze. The patient made an uneventful recovery.

Examination of the appendix showed a small perforation at its tip. The conclusion arrived at after operation was that the appendix lying in the hernial sac had become inflamed, perforated, and the resulting abscess had burst externally. The sac had remained unobliterated, and in it had occurred the strangulation for which the patient was admitted to hospital.

TWO CASES OF HERNIA THROUGH THE TRANSVERSE MESOCOLON.

By F. STRONG HEANEY and G. C. E. SIMPSON, Liverpool.

Rendle Short,[1] in a recent article, summarizes sixteen cases of hernia through the transverse mesocolon. The writers call attention to the following three published cases which are not included by him.

Pringle[2] describes the case of a girl, 5 years old, which is certainly worthy of inclusion: here the opening must have been congenital.

Coffey[3] relates the case of a woman with a twenty years' history, who ten years before the operation had a sudden abdominal pain when carrying a heavy load of wood, following which she had been in bed for some months and had since been a chronic invalid. In this case the intestines traversed the lesser sac and emerged in part above the lesser curvature of the stomach.

P. T. Crymble[4] illustrates a case which he considers might have been a hernia through the transverse mesocolon. The hernia had emerged from the lesser sac through the gastrocolic omentum, but, like Pringle's fourth case, secondary adhesions were so marked that the exact relations were uncertain.

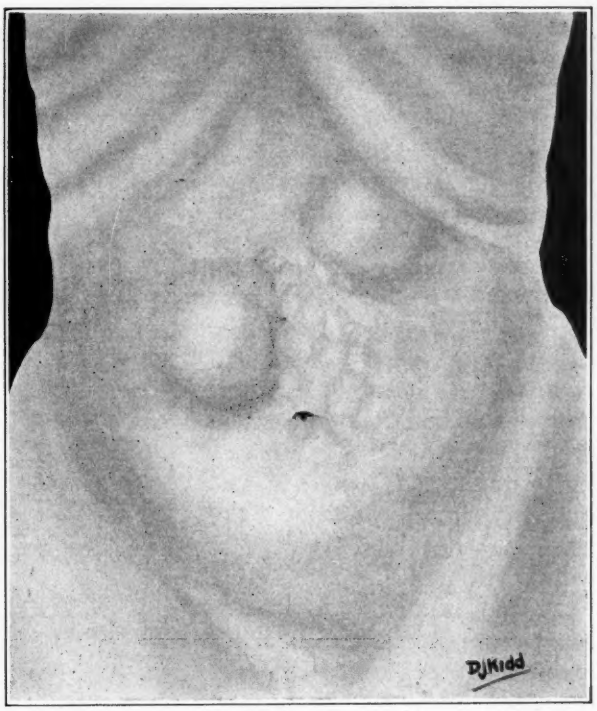


Fig. 263.—*Case* 1. Hernia through transverse mesocolon. External appearance.

The following are two hitherto unpublished cases:—

Case 1 (G. C. E. S.).—A woman, 52 years of age, admitted to the Northern Hospital, Liverpool, in December, 1921, from a tuberculosis hospital. She had suffered from her stomach since girlhood. Twelve months previously she had had sudden *acute pain* in the stomach, and began to suffer more markedly from indigestion. Occasionally she had vomited, and at night brought back some food with a sour and bitter taste.

Examination.—She was extremely emaciated, and her abdomen showed two tumours, one in the upper part of the left abdomen and the other in the right abdomen about the umbilical level (*Fig.* 263). In these peristalsis

was visible from above and the left downwards to the right. Coils of small intestine were apparently overlapping the interval between the sacs.

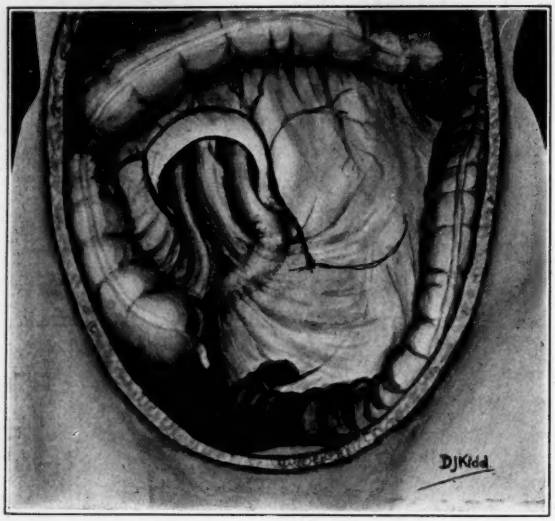


FIG. 264.—*Case* 1. View from below.

OPERATION. — In view of her extreme emaciation and the apparent certainty of the diagnosis of hour-glass stomach X-ray investigations were omitted, and the abdomen was explored; the two tumours were the halves of an hour-glass stomach. Gastro-enterostomy in the upper sac was undertaken in hopes that when the patient was in better condition it would be possible to resect the lower sac. On turning up the colon with a view to carrying out the usual posterior gastro-enterostomy, it was found that there was practically no small intestine in the normal place (*Fig.* 264).

The terminal part of the ileum was soon identified, running a straight course downwards to the ileocæcal angle from a hole in the transverse mesocolon, while at the duodenojejunal junction the intestine continued its vertical course through the mesocolon. Traversing the lesser peritoneal sac, the small intestine emerged again above the stomach and cascaded down to the normal position (*Fig.* 265); both stomach and colon were greatly prolapsed. The intestine was readily withdrawn and brought to the normal position; a gastro-enterostomy was performed, and the hole in the transverse mesocolon sutured.

The patient made a good recovery, and was discharged on Jan. 4. She was re-admitted on March 15 with a view to resection of the pyloric sac,

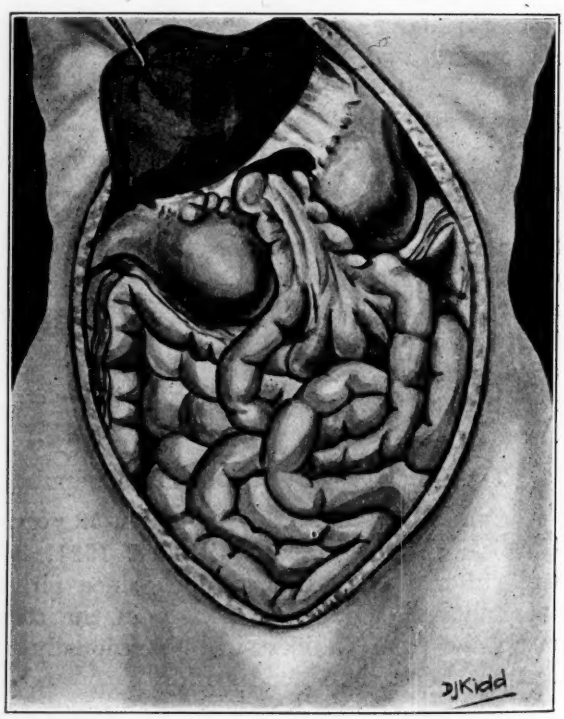


FIG. 265.—*Case* 1. Showing small intestine emerging from gastrohepatic omentum.

but the patient's doctor informed me that before sending her to hospital he had detected tubercle bacilli in the sputum. This observation was confirmed, and skiagrams of her chest lent further support to the diagnosis. Her heart also showed disease, and operative treatment was reluctantly abandoned.

The patient died of heart failure in November, 1922, and by the kindness of Dr. Macwilliam, of Walton Institution, Liverpool, I was present at the post-mortem. The patient had certainly added weight and was much better nourished, and the small intestines were in the normal place. The stomach was still in hour-glass form, the aperture between the two sacs being only about the diameter of a finger. On opening the stomach no signs of an ulcer or the scarring of an old ulcer were detected, although there was duodenal ulceration.

The cause of death was marked 'heart disease'. The specimen is now in the Museum of the University of Liverpool.

Case 2 (F. S. H.).—Mrs. P., age 38, first seen in August, 1923, gave a history of digestive trouble for sixteen years. Eighteen months previously she had a large gastric hæmorrhage and was confined to bed for five weeks. Subsequently she had to remain in bed from time to time for relief of gastric and general abdominal pain. For the last six weeks she had been vomiting after food, vomiting when she tried to walk, and in pain at all times save when lying down.

For years, concurrently with her other symptoms, she had suffered from constipation. She had tried to wear a visceroptosis belt, but it aggravated her epigastric pain.

Examination.—She was very emaciated, had a long thorax, narrow in its lower part, a narrow subcostal angle, and a bulging lower abdomen—the figure of the infantile type of visceroptosis. The abdomen was tender to pressure, especially in the epigastrium.

An X-ray examination which had recently been made by Dr. Swanson Hawks showed an hour-glass stomach (*Fig.* 266) and marked ptosis of the stomach and large intestine. The hepatic flexure was low, and the first part of the transverse colon passing down to the pelvis could not be manipulated free of the cæcum (*Fig.* 267). The middle part of the transverse colon lay in the pelvis looped on itself (*Figs.* 267, 268). There was considerable large bowel delay.

Operation.—The small intestines were seen emerging from a large transverse opening in the gastrocolic omentum. Above this opening lay the hour-glass stomach, and in the pelvis was the transverse colon lying behind the small intestines. The great omentum had almost disappeared, being represented by a few tags of fatty tissue forming weak adhesions at two or three points in Douglas's pouch. These were easily broken down, and when the transverse colon was lifted up the small intestines passed back through the gastrocolic omentum and the transverse mesocolon without difficulty.

The lower sac of the hour-glass stomach had an active ulcer on its posterior wall eroding the pancreas. This part of the stomach, together with the constriction, was resected, and the operation completed by the anterior

Polya method. The short loop of jejunum thus supported the transverse colon. The remains of the great omentum were sutured to the gastrohepatic omentum and to the stomach in order to prevent the transverse colon sliding to right or left across the loop of jejunum.

When last heard of three months ago she was quite well. The constipation was relieved as well as the stomach symptoms.

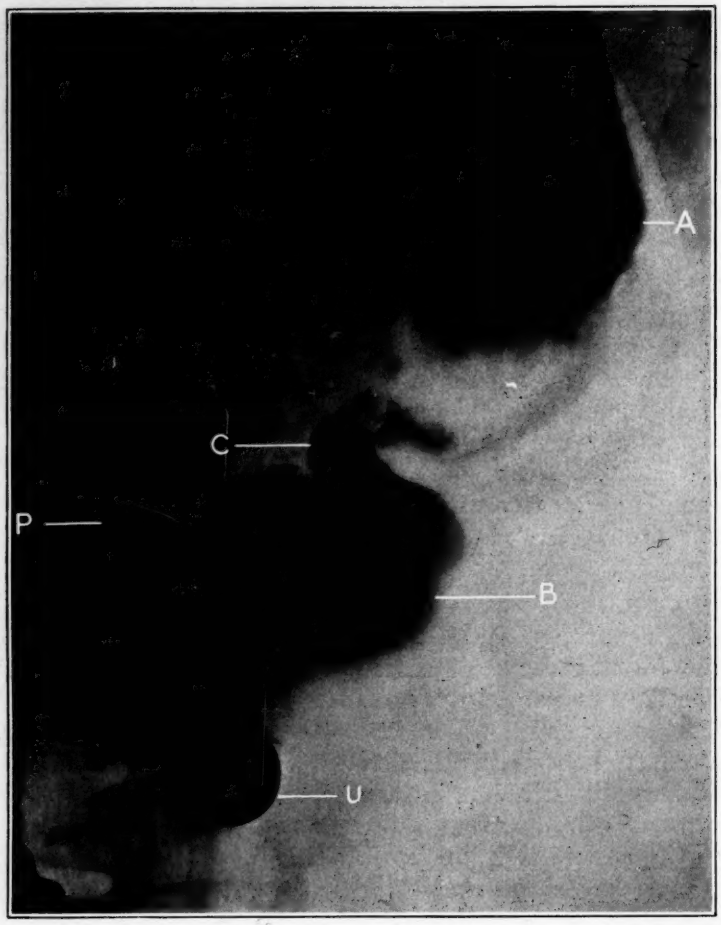


FIG. 266.—*Case* 2. Skiagram after opaque meal, patient horizontal, showing hour-glass stomach. A, Upper segment; B, Lower segment; C, Constriction; P, Pylorus; U, Umbilicus.

Of the above 21 cases of hernia of the small intestines through the transverse mesocolon, in 1 case the intestines emerged through the foramen of Winslow; in 8 cases the hernia passed out through the gastrohepatic omentum; and in 3 it passed the gastrocolic omentum; in the remaining cases the hernia stayed in the lesser sac. In 14 cases gastric or duodenal ulcer or carcinoma was present; in 2 there was organic hour-glass stomach, and in 2 others spasmodic hour-glass stomach. In at least 10 cases there was visceroptosis. Of 14 where we have been able to discover the sex, 13

were females and 1 only was a male. The ages, if we except Pringle's seventh case in a girl of 5, varied from 26 to 60 years.

The first of the two cases now recorded resembles Coffey's case in that an acute abdominal crisis seemed in each to mark the point of time at which the mesocolon gave way. The second is the only recorded clear case of the intestines emerging from the lesser sac through the gastrocolic omentum.

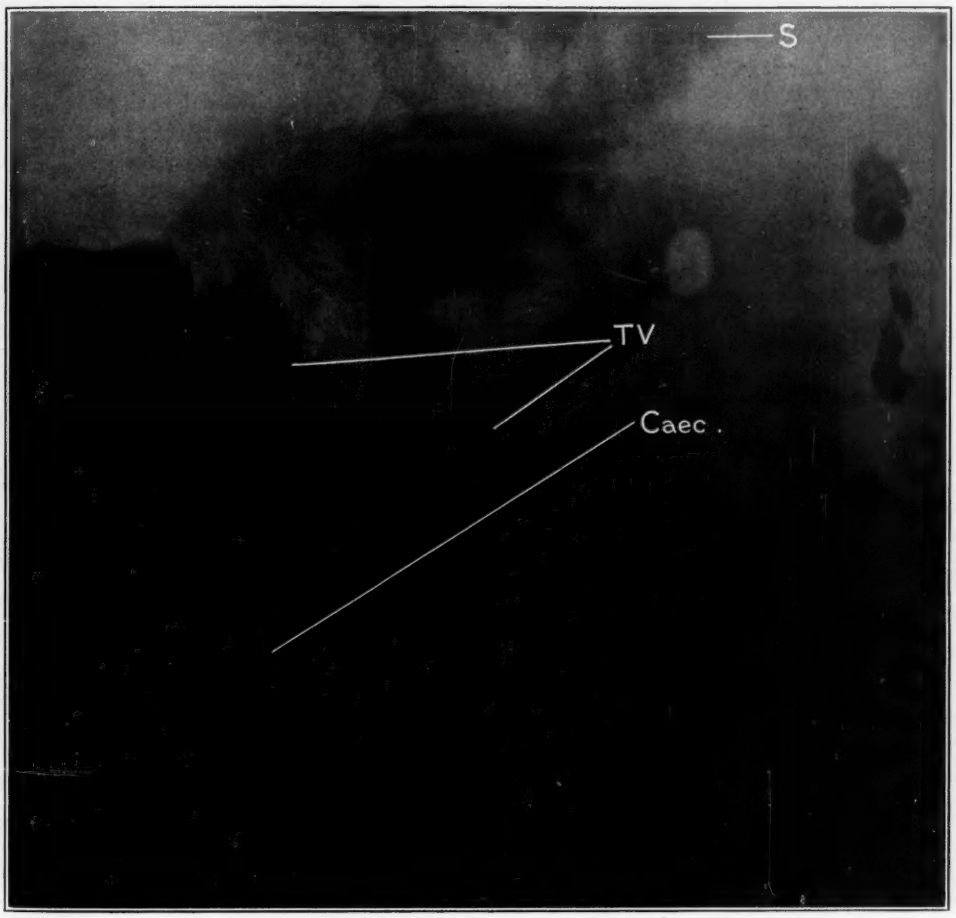


FIG. 267.—*Case* 2. Twenty-four hours after opaque meal, showing relation of cæcum (Caec.) to transverse colon (TV) and looping of latter on itself. It was impossible by pressure to straighten out the loop in the colon or to raise it sufficiently from the cæcum to be sure there were no adhesions. The stomach (S) still contained a trace of opaque meal.

Two other cases are mentioned in the literature, but the relations were uncertain owing to adhesions.

Apart from the rarity of our two cases the question of causation is of interest. Many causes have been suggested: retroperitoneal pouches, congenital defects of the mesocolon, violence, and ptosis. Pringle[2] and Chalmers[6] suggest that these herniæ develop by way of the intermesocolic pouch, with secondary rupture into the lesser sac.

A case of intermesocolic pouch recently came under the observation of one of the writers. The anterior margin of the orifice was firm and unyielding, and capable of strangulating any gut within the pouch. We feel that if the 22 cases of hernia into the lesser sac had developed by secondary rupture from this pouch a number of cases of strangulation would also be on record.

The strength or weakness of the transverse mesocolon cannot be of much importance. Although fenestration is rare, the structure is at best flimsy,

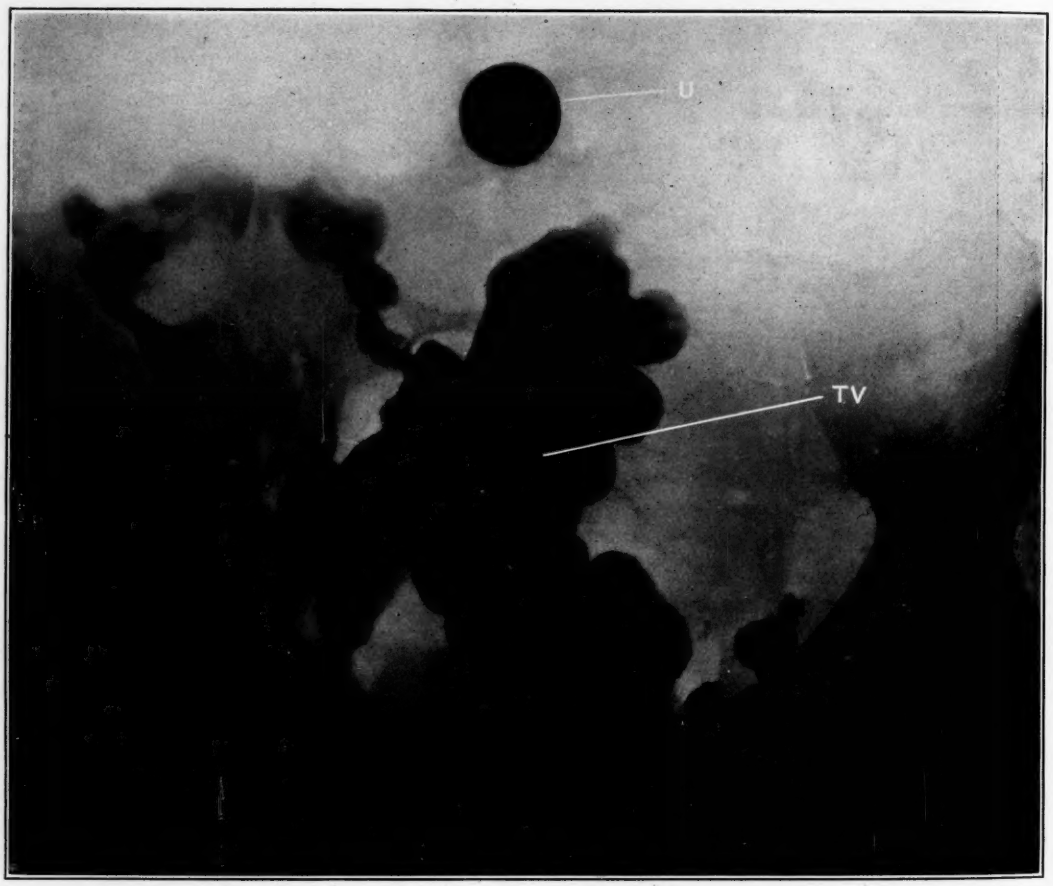


FIG. 268.—*Case* 2. Seventy-two hours after opaque meal. The lower bowel had been cleared by enema. The transverse colon (TV) is still filled and looped on itself.

and incapable in itself of retaining the small intestines in their proper compartment of the abdomen. Security depends on equality of pressure on either side of this membrane.

It is generally recognized that mid-line ptosis predisposes to ulcer and hour-glass stomach. We consider it the all-important factor in the production of hernia through the transverse mesocolon. Coffey noted it in one case, Mayo in two ; in fact it was definitely present in 10 of the 21 cases, and the remaining cases were females of an age and with a history at least consistent with the presence of visceroptosis.

It is easy to visualize the mechanism of the hernia. In the normal abdomen the relationship of the stomach and colon on the one hand and the small intestines on the other is such that when there is a sharp rise in intra-abdominal pressure, as, e.g., in vomiting, the stomach and colon are thrust more firmly into the upper compartment of the abdomen, and there support the transverse mesocolon against the upward pressure of the small intestines. If the stomach and colon are prolapsed, not only is this support lacking, but the weight of these viscera crowds the small intestines upwards under the stretched transverse mesocolon and increases their upward thrust in expulsive efforts—with possible rupture.

The direction which the small intestines will take on reaching the lesser sac will be determined by such considerations as the length of the gastrocolic omentum, the presence or absence of adhesions on the posterior aspect of the stomach, and the extent to which the stomach itself has prolapsed.

Two further points deserve mention: (1) Seeing that mid-line ptosis so commonly accompanies hour-glass stomach, in dealing with the latter there is a *prima facie* reason for preferring the anterior to the posterior operation (whether Polya or gastrojejunostomy), as in the anterior method the prolapsed colon is supported by the jejunal loop; (2) It is probable that hernia into the lesser sac arising after gastro-enterostomy occurs only in the presence of ptosis.

REFERENCES.

[1] Short, A. Rendle, *Brit. Jour. Surg.*, 1925, Jan., xii, 456.
[2] Pringle, J. Hogarth, *Glasgow Med. Jour.*, 1919, xci, 129 (*Case* vii).
[3] Coffey, *Surgical Monographs: Gastro-enteroptosis*, 1923, 208.
[4] Crymble, P. T., *Quain's Anatomy*, 11th ed., ii, part 2, *Fig.* 349.
[5] Stolzenberg, *Virchow's Arch.*, 1910, ccx, 470.
[6] Chalmers, *Jour. Pathol.*

AN UNUSUALLY LARGE TUMOUR OF THE RIGHT BREAST.

By W. E. TANNER, London.

The patient, a married woman, age 53, who had had ten children, was seen in September, 1924. She said that the right breast had been gradually getting larger for seventeen months, that during the last month it had rapidly increased in size, and during the last week there had been much watery discharge from the right nipple.

On Examination.—A stout woman of healthy appearance. In the right breast was a large tumour apparently arising in the upper part of the breast (*Fig.* 269). There were irregular rounded projections springing from the tumour, particularly in its upper part. The nipple was not retracted, and, with the lower part of the breast, was pushed downwards and forwards by the tumour. The skin was not attached, and was normal in appearance except over the upper part of the tumour, where it was thinned by pressure and the fluctuating projecting masses appeared blue through the thinned skin. The tumour was freely movable on the chest wall, and no enlarged glands could be felt in the axilla or above the clavicle. The mediastinum

was clear, and nothing abnormal was detected in the other systems of the body.

A diagnosis of Brodie's serocystic tumour of the breast was made; the patient was advised to have the right breast removed, and a good prognosis was given. The breast was excised on Sept. 25, and weighed 18 lb. She made a good recovery and has had no complications of the breast condition. In March, 1925, a large gall-stone was removed from the gall-bladder.

DESCRIPTION OF THE TUMOUR.—I am indebted to Mr. T. H. C. Benians for the following description of the macroscopical and microscopical structure :—

"The tumour is rounded, with irregular rounded bulging areas mostly at the upper part. The skin is normal in appearance for the most part, but thinned and bluish over some of the upper projecting masses; it moves freely over the whole tumour. The nipple is slightly projected, but is not adherent.

FIG. 269.

"A vertical section through the middle of the tumour shows a thin layer of fat and subcutaneous tissue between skin and tumour; the tumour bulges freely towards the cut surface, especially in its central parts. Towards the skin surface, and in most parts immediately at the margin of the tumour, is a deep cleft bounded by a thickened membrane which is apparently a cyst wall with numerous cyst cavities opening out of it, so that the bulk of the tumour is lying inside a multilocular cyst. The cyst wall is white and tough, and in parts covered by thickened white and yellowish patches. The cyst also contains whitish-yellow semi-fluid and granular material, which is made up of cholesterin and degenerate matter. The tumour projecting into the cyst is smooth and white or pinkish on section, but on its free surface, which is nodular, it has a clear mucoid appearance in parts, in other parts an opaque white almost cartilaginous look, although soft to cut, and other parts are

covered with dilated capillaries. No large vessels are to be seen, and there are no hæmorrhages.

"Sections cut from various parts of the tumour present a varying histological picture. The bulk of the tumour which formed the intracystic masses is composed largely of spindle cells, and these vary greatly in type and in arrangement. In parts they are large, deeply staining, and fitted closely against each other; the nuclei of these cells are relatively large in comparison with the cytoplasm. In parts the cells are more elongated, with rod-shaped nuclei, and are more of the type of adult connective-tissue cells. In a still further variation the cells are myxomatous in type, with small or larger clear areas between them; this myxomatous change affects a large part of the tumour. Irregularly interspersed throughout the mesoblastic tissues are gland tubules lined with a cubical epithelium, and in places these are dilated into small cysts. In some parts, and more particularly in areas showing gland tubules, are numerous irregular structureless areas apparently derived from a hyaline degeneration of the tumour cells. Blood-vessels are scarce but well formed.

"Sections of the small part of breast tissue outside the tumour show an increase of fibrous tissue and some lobular hyperplasia. The fibrous tissue is more dense towards the free surface where it constitutes the cyst wall. The epithelial lining covering it varies in different parts from a single layer of cubical cells to a stratified layer half a dozen cells in thickness; these epithelial cells are largely degenerate and show no nuclei."

Dr. G. W. Nicholson, Morbid Histologist to Guy's Hospital, who very kindly examined the sections, reports as follows: "The sections examined were from the edge of the tumour and show the structure of a fibro-adenoma, the connective-tissue matrix of which is composed of whorls of spindle cells, some of which have undergone hyaline change. They surround spaces lined by glandular epithelium. The surrounding breast is compressed, and forms a capsule for the tumour."

In the *Medical Times* for 1844 Sir Benjamin Brodie gives a description of two similar cases. He says that the disease is often confounded with carcinoma, and is not met with in hospital practice, but often shows itself in private life. In the first patient the tumour was about the size of a walnut. It was punctured, found to contain serum, and then laid open with a lancet. A year later a fungous tumour was found where the cyst had been opened. The breast was amputated, and was made up of cysts containing fluid matter. A solid tumour projected from the inner surface of the largest cyst. In the second case the breast on removal was found to weigh between 7 and 8 lb. He states that the skin does not always ulcerate in these cases, but occasionally it is so distended that it bursts. In conclusion he says: "I have given no name to this affection, because I think it is an error of modern times to be continually giving new names to diseases, but if it must have a name I think it should be called serocystic tumour."

REVIEWS AND NOTICES OF BOOKS.

Clinical Researches in Acute Abdominal Disease. By ZACHARY COPE, B.A., M.D., M.S. (Lond.)., F.R.C.S. (Eng.), Senior Surgeon to Out-patients, St. Mary's Hospital; Surgeon, Bolingbroke Hospital, etc. Demy 8vo. Pp. 148, with 31 illustrations. 1925. London: Oxford Medical Publications. 12s. 6d.

THE work consists for the most part of an expansion of the Arris and Gale Lecture, 1922, publications in the *Lancet*, 1924, and in the BRITISH JOURNAL OF SURGERY and *British Medical Journal*.

Chapter 1 deals with the scope of clinical research, and the author suggests that in clinical research it is not necessary for two workers to collaborate as it is in experimental work from a laboratory, as the means of verification of opinions offered in clinical research are near at hand for everyone to test. Since reading this book, and on many occasions before, we have applied the suggestions put forward and have found them of the greatest possible help in many cases. The three main purposes to which clinical research may be directed are: (1) It is within the scope of the clinician to test with thoroughness the results achieved by work in the laboratory. (2) It is within the scope of clinical research to try various empirical methods, and to furnish the results to the laboratory for explanation and elaboration. (3) It is within the scope of clinical research also to record and compare clinical facts with the object of determining some questions which are inaccessible to laboratory methods of study. The author gives five rules which he says should be observed if clinical research is to be of any value.

In the chapter on the function of the parietal peritoneum two areas of peritoneum are described; one, the demonstrative area, which includes all the lining of the abdominal cavity except the pelvis and the central and inferior part of the posterior abdominal wall; and the other, the non-demonstrative or silent region, which comprises the pelvis and that part of the posterior abdominal wall bounded by the ascending colon, descending colon, and the transverse mesocolon. It is suggested that the non-demonstrative area is probably supplied via the sympathetic system and the demonstrative from the main somatic nerves. Stimulation of the non-demonstrative areas does not give rise to any clinical localizing symptom or sign. For this reason an acutely inflamed appendix either in the pelvis or behind the lower end of the ileum may give rise to no sign of irritation, and may be present with entire absence of muscular rigidity. A point which should be thoroughly realized is that rigidity of the abdominal wall is not necessarily present in acute appendicitis, and that when this is not present the appendix is usually found in the pelvis or behind the lower end of the ileum.

Chapter 4 is illustrated by drawings of areas of hyperæsthesia found in acute appendicitis, perforated gastric and duodenal ulcers, cholecystitis, etc. It cannot be taken as an indication of the existence of any particular lesion, but of an irritative condition being present in the area supplied by that particular segment of the cord.

Phrenic shoulder-pain is described at length, its presence in acute abdominal disease, and its usefulness as a method of differential diagnosis between disease in the abdomen and in the thorax. Chapter 6 is devoted to the differential diagnosis of abdominal and thoracic disease, and a general summary of the different signs and tests is given in a comparative table.

A particularly interesting chapter is that dealing with the differential diagnosis of genito-urinary symptoms in acute appendicitis. There is no doubt that innocent appendices have been removed in many cases of stone in the right ureter.

A new test—the femoral test—is described in Chapter 7: inflammation of the peritoneum over the external iliac vessels causes pain in the hypogastric region

when pulsation in the femoral artery is stopped by pressure in the thigh ; this sometimes proves of value in determining the position of an acutely inflamed appendix.

The book is well arranged, and the drawings are simple and clear. Every chapter contains suggestions of great interest which will undoubtedly help the surgeon in differential diagnosis. This latter is a subject which we think needs emphasis, as many are inclined to be satisfied when they have decided whether an abdomen should be opened or not. For those who take a deeper interest in their work this book will prove of the greatest help.

Minor Surgery. By LIONEL R. FIFIELD, F.R.C.S., Surgical First Assistant and Registrar, London Hospital ; Demonstrator of Minor Surgery, London Hospital. Crown 8vo. Pp. 431 + x, with 273 illustrations. 1925. London : H. K. Lewis & Co. Ltd. 12s. 6d. net.

IN this book the author has endeavoured to give an account of minor surgery as taught at the London Hospital, and he is to be congratulated on the result, which does great credit not only to himself but also to the London Hospital Medical College.

Surgery, wherever it is taught, should be essentially the same, though details may vary according to individual taste or custom ; and whether major or minor surgery be considered, the great underlying principles cannot alter or vary. Teaching, especially the teaching of students in their earlier years, should be systematic, though it is well for them as the time comes for qualifying and assuming responsibility that they should have a knowledge of the practical experience of their seniors, so that they may have some guide to the most efficacious forms of treatment and be able to give a reasonably accurate prognosis in the cases they are likely to meet in practice. This little book, under the modest title of *Minor Surgery*, treats of the great principles as well as the details of minor operations ; and, while being systematic to a degree, gives valuable advice in the choice of alternative methods of treatment and also in the results which may be expected from them.

A great deal of material of doubtful value which used to appear in book after book has been omitted, and this has enabled the author to emphasize the things he considers most important, while confining himself strictly to surgical conditions which, however great their importance, could not be termed major surgery. To discriminate between major and minor must often have been difficult, but the author's judgement has been well considered. He refers frequently to his own experience, but also quotes freely from the writings and practice of well-known surgeons whose work has enriched the science and art of surgery in recent years, thus bringing the book absolutely up to date.

The early chapters give an account of the routine examination of a patient, the acute abdomen, acute intestinal obstruction, antiseptic and aseptic technique, and the methods of sterilization of instruments and materials. Preparation for operation and operative technique are well described ; and after-treatment, including the treatment of shock and other complications, is then considered. A slight error here is that massage is mentioned in the treatment of venous thrombosis with insufficient warning.

We then pass to chapters on wounds, hæmorrhage, cellulitis, and abscess, all of which are full of sound practical teaching. Chapter 7, on infection of the hand, gives a résumé of the work of Kanavel, to whom the author pays tribute. The section on bandaging is useful in that it includes only the methods most commonly used. The chapter on minor operations contains an astonishing amount of information and is well illustrated. The section on fractures is admirable, because it includes an account of the after-treatment of the fractures of each bone, and the prognosis and probable period of incapacity. With the dislocations is included a brief but satisfactory account of internal derangements of the knee-joint.

The chapters on diseases of joints, genito-urinary affections, and trusses, and the short chapter on the eye, require no comment except that they maintain the standard of the earlier parts of the book, which ends with a chapter on the administration and choice of anæsthetics. Apart from a number of printer's errors the book is well produced, and it can be confidently recommended as being of value in the teaching, study, and practice of minor surgery.

Some Encouragements in Cancer Surgery. By G. GREY TURNER, F.R.C.S., Hon. Surgeon, Royal Infirmary, Newcastle-upon-Tyne. Pp. 75, with 40 illustrations. 1925. Bristol: John Wright & Sons Ltd. 7s. 6d. net.

THIS little book is a record of some cases of malignant disease operated on by the author, and contains forty excellent illustrations of the specimens removed. The cases are examples of cancer from all the common sites, and many are instances of advanced disease. Mr. Grey Turner has followed up these cases in order to determine the length of life after operation and the cause of death, and the book has been written to encourage surgeons to persevere in efforts to relieve, and at times to cure, patients suffering from what appear to be, in many instances, very unfavourable growths from the operative point of view.

He is fully alive to the advantages of operating in the earliest possible stage of the disease, but he points out, and we think rightly, that a long history often means a good resistance on the part of the patient, and that a formidable lump, under these circumstances, does not necessarily deprive the patient of the possibility of being cured by a sufficiently determined effort on the surgeon's part. There is an inclination in the minds of quite a number of the profession to regard all operations for malignant disease as doomed to failure, irrespective of the stage at which the patient is seen, of the fight he may have put up against the disease as evidenced by the duration of the symptoms and the general well-being in spite of a large local lesion, and of his desire to take what is, after all, his only chance of getting rid of the disorder. We recognize that this gloomy outlook is not seldom justified by events, but we recommend those who suffer from this hopeless attitude of mind to read this book of Mr. Grey Turner's, and to revise their antipathy to operation, for they will find reliable records of patients living many years who would inevitably have been dead of their disease years before, and moreover who, when they did die, succumbed to something quite unconnected with the cancerous growths for which the operations were performed.

Mr. Grey Turner says in his book that in his opinion every case which does not show unequivocal evidence of dissemination should have the chance which only an operation offers, and in our view this is the only justifiable advice to give patients suffering from this disease at the present time. It is the unanimous opinion of all those who know anything about malignant disease that it is in the first place a local lesion, and probably remains so longer than we think, and that it can always be removed entirely if the attempt be made before dissemination begins. It is only by adopting an optimistic attitude towards the operative treatment of malignant disease that we, as a profession, can hope to induce patients to come earlier and yet earlier for treatment, and this is the key to the situation from the curative point of view.

If Mr. Grey Turner's book does anything towards converting the pessimists of the profession it will have achieved a most useful purpose, and we feel that a careful study of the cases recorded cannot have any other effect on an unbiased mind.

Cancer and the Public: The Educational Aspect of the Cancer Problem. By CHARLES P. CHILDE, B.A., F.R.C.S., M.R.C.P.E.; President B.M.A., 1923; Chairman of Public Health Committee, Portsmouth; Consulting Surgeon, Royal Portsmouth Hospital. Demy 8vo. Pp. 267. 1925. London: Methuen & Co. Ltd. 10s. 6d. net.

THIS book is intended both for the general public and for the medical profession. In an introductory chapter the author adduces good reasons for thinking that the subject of cancer and what can be done for it by timely and suitable surgery should be brought prominently before the public. Whatever view may be taken of this debatable subject, it is well that a book of this kind should be written by one who has wide knowledge and ripe experience and who is capable of clear reasoning and cool judgement in this important matter.

The book deals solely with carcinoma, and especially with carcinoma occurring in certain definite situations, and with the prospects of its cure by surgical removal. Sarcoma is excluded from the scope of the book.

In an amusing and well-written chapter on cancer theories, the author discusses briefly the numerous theories that have been brought forward, both by the profession and by the laity. He shows how shallow are the arguments by which most of

them are supposed to be supported. He pours quite justifiable ridicule on the idea that articles of diet, or intestinal stasis, or lack of vitamins, are likely to have anything to do with its production. He does not consider that climate, locality, occupation, or mental worry, all of which have their advocates, have anything do with the causation of cancer. Although rightly laying stress on local irritation as a frequent determining cause, he wisely concludes by saying that the " riddle of its cause has not been solved ".

Various cancer fallacies held by the public are then discussed, followed by seven prominent 'facts', at five of which no surgeon is likely to cavil. The first and third, however, although possibly true, can scarcely be said to have been proved. The inferences to be drawn from these facts are then related. The curability of cancer, the condition of cure, and the possibilities of cure are then ably and temperately discussed, with abundant illustrative statistics.

What the public should know about cancer, its danger signals, and the means to be taken for its cure, are dealt with at some length. The American campaign against cancer is contrasted with the apathy shown on this side of the Atlantic. A more thorough education of the public on the known facts of cancer and the hopefulness of cure in cases which are seen early is strongly advocated.

After a short chapter on radiotherapy, its limitations and uses, the author concludes very sensibly by saying that his object has been to " draw attention to the educational aspect of the cancer problem; to brush away former errors; to show that cancer is capable of being dealt with successfully by surgical operation at the present time, and that it is the only method we possess of treating it hopefully; but that the very condition of success lies in that knowledge on the part of its victims which will enable them to avoid delay in seeking advice. My purpose has been to demonstrate that until surgeons are enabled to come face to face with cancer in its earliest beginnings, its treatment by operation must remain generally ineffectual, only exceptionally curative; that education is essential to and must precede successful treatment; that as long as people apply as they do now for the first time with advanced cancer, so long will the results of its treatment spell failure " (p. 258).

A blemish in what is otherwise a good book is the unnecessary, and, as many will think, the totally unwarranted comparison of cancer with acute appendicitis (pp. 111, 113, 189). To say that a patient with an acute perforated appendix unless immediately operated upon cannot avoid " certain death " is at least a gross exaggeration. Many thoughtful and experienced surgeons and physicians at the present day know better than this. In any case, even if the statement were true, it has no bearing on cancer, and had better have been omitted, especially as it is likely to cause the well-informed reader to suspect, although quite undeservedly, the otherwise cool judgement of the author.

The book is well written and is easy to read, although there is perhaps a little too much repetition in places. For example, on p. 154, we read again much of what has already been said on p. 4. Misprints are very few, but there is an obvious one in a Latin quotation on p. 113, and another on p. 149 in the German title of a book, which, however, is correctly spelt in the table of references on p. 261.

Fractures and Dislocations: Immediate Management, After-care, and Convalescent Treatment, with Special Reference to the Conservation and Restoration of Function. By PHILIP D. WILSON, M.D., F.R.C.S., Instructor in Orthopedics, Harvard Medical School; and WILLIAM A. COCHRANE, F.R.C.S. (Edin.), Tutor in Clinical Surgery, Edinburgh University. Pp. 789 + xv, with 978 illustrations. 1925. London: J. B. Lippincott & Co. 45s.

THIS is certainly one of the best works on fractures and dislocations which has appeared in recent years. Not only is it the joint work of an American and a Scotchman, but it also represents the generally accepted principles of treatment of the members of the staff of a large general hospital (Massachusetts). In this institution all fractures are looked after by a special 'Fracture Service', consisting of six surgeons, four of these being 'general' surgeons and two being orthopædic. This ideal arrangement, the adoption of which is long overdue in the hospitals of

this country, makes it possible to come to some general agreement about the most practical and successful methods of treatment. The present work represents the outcome of such an agreement.

Ample space is devoted to general considerations, and especially to those of anatomy and physiology. The treatment of each type of injury is described in a very practical manner, and followed up until complete functional restoration has been achieved. Methods of splinting are reduced to the simplest possible terms, full value being ascribed to the various patterns of Thomas and Jones, and also to plaster-of-Paris and traction devices. The book is intended mainly as a guide to the student and general practitioner, and therefore most stress is laid upon non-operative methods. The indications for open operation are mentioned—perhaps with a rather conservative bias—but the details of operation are omitted.

In addition to those on fractures and dislocations of the limb bones and joints, there are chapters dealing with fractures of the spine and of the facial bones. The former is very valuable, the latter less so.

The great value of the book consists in its wealth of practical details, all of which represent the considered opinion of a large group of experienced surgeons. The profuse illustrations greatly help the elucidation of the text; in fact the figures alone are almost a complete treatise. The chief criticism of the work is that the open operations are put too much in the background, and even when mentioned are not described.

The Principle of Early Active Movement in Treating Fractures of the Upper Extremity. By J. W. Dowden, M.B., F.R.C.S.E., Surgeon to Chalmers Hospital; late Surgeon to the Edinburgh Royal Infirmary. Large 4to. Pp. 111 + xvi, with numerous plates. 1924. Edinburgh: Oliver & Boyd. 16s. net.

This volume consists of a number of reproductions of X-rays and photographs of fractures of the arm in various stages of treatment. The letterpress is sketchy, and serves to do little more than explain the various pictures. The method certainly contravenes a well-accepted principle, that immobilization should be continued until callus is sufficiently strong to maintain the fragments in order to restore positions. It appears from the letterpress that the author pays no particular attention to the reduction of displacement by manipulation under an anaesthetic and checked by X rays; yet, as far as can be judged in the notes, the treatment seems to be followed by good functional results; how large a part in this is played by the persuasive personality of the author or by the hardihood and insensibility to pain of his Edinburgh patients, this is not the place to judge. It is possible—in fact, to the reviewer probable—that Mr. Dowden claims too much for this line of treatment; but we would agree with him that there is much to be said for the use of active movement in the after-treatment of fractures, just as there is much to be said against the use of passive movements, and if this volume directs attention to this principle it can only do good.

The reproductions are well done, but the author falls into a common mistake in describing various radiograms as "separations of the lower humeral epiphysis" which are really those of supracondylar fractures.

Anæsthesia. By James Tayloe Gwathmey, M.D., First President of the American Association of Anæsthetists; with collaborators on special subjects. Second revised edition. Royal 8vo. Pp. 799 + xxv, with 273 illustrations. 1924. London: J. & A. Churchill. 25s. net.

In his new edition Dr. Gwathmey has produced a comprehensive account of the specialty as practised to-day; owing to recent progress, he has found it necessary to delete chapters on such subjects as electrical anæsthesia and statistics in order to make room for more important and practical material. In the introductory section the history of anæsthesia is fully and delightfully told. In the second chapter the physiology of the various methods is put shortly but exceedingly clearly. The author has entrusted the description of some of the subjects to a number of collaborators who are recognized authorities on the methods concerned, such as Elsberg on intratracheal insufflation, and so forth.

Dr. Gwathmey's capacity for combining the practical with the theoretical has enabled him to produce an exceptionally reliable chapter on each of the standard anæsthetics—chloroform, ether, gas, and ethyl chloride, and the reader is left with a clear mental impression as to their respective uses and modes of employment.

Local anæsthesia has been allotted a quite prominent position in this book, and in referring to the advantages to be derived from combining local with general anæsthesia the author seems to suggest that there is room for improvement in the training of the surgeon for his share in this valuable practice.

The book is well got up and efficiently illustrated, and cannot fail to become a favourite with specialist and student.

Local Anæsthesia: its Scientific Basis and Practical Use. By Prof. Dr. HEINRICH BRAUN, Zwickau. Translated and edited by MALCOLM L. HARRIS, M.D., Professor of Surgery, Chicago Polyclinic. Second American from the sixth revised German edition. Royal 8vo. Pp. 411 + xxi, with 231 illustrations in black and colours. 1924. London: Henry Kimpton. 25s. net.

IN view of the widespread and increasing interest in and employment of local anæsthetics, the appearance of another edition of this comprehensive standard text-book is most welcome.

The first eight chapters deal with the theoretical side of local anæsthesia, and include a detailed account of the characters and properties of the various drugs which may be used for its production. A notable addition to this section is a fuller treatment of the subject of poisoning by novocain. Chapters 9 and 10 give a general account of the technique of the various methods of application of local anæsthetics, and a useful section on their value and indications for their use. There is a very well illustrated description of lumbar and sacral anæsthesia, which is one of the features in which this edition excels its predecessors.

The remaining half of the book is devoted to descriptions of the exact method of inducing anæsthesia for operations on the head, neck, trunk, and extremities. In fact, extremely few of the operations of surgery are omitted, so that the possibilities of local anæsthesia are very fully set forth. We cannot but remark that although almost any major surgical procedure may be carried out under this form of anæsthesia, yet its application must be limited by the individuality of the surgeon and the patient. The illustrations, in black and colours, are excellently clear, but even they emphasize the fact referred to above—that the 'strain' upon patient and surgeon must be exceedingly severe in some cases, and that what is possible under local anæsthesia may not always be quite advisable.

For those who wish to explore the field of local anæsthesia, this book may be recommended as giving a comprehensive description of the subject, with large numbers of references to the practical experience of the author and other writers.

The Technic of Local Anæsthesia. By A. E. HERTZLER, A.M., M.D., Ph.D., LL.D., F.A.C.S., Professor of Surgery in the University of Kansas. Third edition. Imp. 8vo. Pp. 272, with 140 illustrations. 1925. London: Henry Kimpton. 25s. net.

A COMPREHENSIVE work describing in detail the technique for the employment of local anæsthesia in almost every operation that the surgeon is called upon to perform. A general review of the whole subject is followed by a detailed account of the more commonly undertaken operations. The directions given are simple and easy to understand, the plan followed being to describe briefly what the surgeon sets out to do and how he can best carry it out under local anæsthesia. Some of the more ambitious procedures are dismissed briefly, and it is pointed out that the simpler operations should be mastered, and then as the surgeon gains confidence in himself the more difficult ones can be added to his list. If he is to be successful, the operator must have perfected his routine by experiment on the cadaver before he employs it on a patient. Stress is laid on the giving of an occasional word of encouragement to a patient who is undergoing a great mental strain.

Local infiltration and field blocking are described as the methods of choice, being preferred to paravertebral anæsthesia or the blocking of individual nerves,

the reasons given being that they are more certain in their action and that they may have to be employed to supplement the latter procedures when they are used.

The use of quinine is advised on a more extensive scale than has hitherto been practised, and from the author's experience seems to merit a more prolonged trial than has been accorded to it in the past.

Throughout the book the style is good, the description clear and simple, and altogether it is to be recommended to those who desire a small handbook dealing with the whole subject of local anæsthesia.

The Westminster Hospital Reports. Vol. XIX, 1924. Edited by E. Rock Carling and Hildred Carlill. Pp. 299 + xxvi, illustrated. London: Henry J. Glaisher. 7s. 6d. net.

The *Reports* of the Westminster Hospital have been discontinued for ten years, and this is the first of the new volumes. It was hoped to present a systematic study of the post-mortem records for the last ten years; but such a plan was found to be impossible, and the present volume consists of a haphazard collection of individual contributions, only the first six of which form part of the original concerted plan. Sir Edward Pearson contributes a foreword, in which he expresses an opinion favourable to the efficiency of the Voluntary Hospital system. On the face of it, it would appear that the haphazard appearance of scientific reports would hardly be the occasion for this tribute.

The book, though small, is full of interest from cover to cover. As a kind of celebration of the rebuilding of the hospital, Mr. Spencer has written a most fascinating section about the history and growth of the old institution. Then follow six chapters devoted to the post-mortem records relating to special subjects. Mr. Spencer writes the section dealing with the mouth and tongue, pointing out the importance of pulmonary complications in causing a fatal issue. Mr. Turner deals with gastric and duodenal ulcers, of which there had been 370 cases, with a mortality of over 10 per cent, the duodenal cases having a higher mortality than the gastric. Mr. Pinto Leite writes on the post-mortem evidences of lung complications due to general anæsthesia, and he finds no evidence that ether or closed ether is more dangerous in respect to its effect on the respiratory apparatus than other anæsthetics. Mr. Braxton Hicks analyses the cases which came before the coroner; Dr. Goodwin discusses the toxæmias of pregnancy; and Mr. Rock Carling describes 19 cases of fatal pulmonary embolism. The rest of the volume consists in short papers and in statistical tables.

Guy's Hospital Reports. Vol. LXXIV (Vol. IV, Fourth Series), No. 4, October, 1924. Edited by Arthur F. Hurst, M.D. Medium 8vo. Pp. 121, with 49 illustrations. 1920. London: Wakley & Son. 12s. 6d. net.

Guy's Hospital Reports continues to provide a number of papers from members of the staff, and the present number contains observations on cases of Addison's disease, articles on methæmoglobinæmia, arachno-dactyly, and several other subjects. There is a paper on deep X-ray therapy, from which one hoped it might have been possible to have obtained some accurate knowledge of the value of this treatment; presumably this is too early to be expected, for the article deals almost entirely with the details of technique, and not with results.

A Synopsis of Surgery. By Ernest W. Hey Groves, M.S., M.D., B.Sc. (Lond.), F.R.C.S., Surgeon to the Bristol General Hospital; Professor of Surgery, University of Bristol. Crown 8vo. Pp. 671 + viii, with 164 diagrammatic illustrations. 1925. Bristol: John Wright & Sons Ltd. 17s. 6d. net.

This seventh edition, enlarged and revised, now contains 671 pages and many line illustrations. It is a synopsis of surgery, as the Preface states, but this synopsis is now becoming as large as the text-books themselves of thirty years ago. The fact that this work has gone through seven editions is sufficient guarantee that it is wanted, and though some teachers do not see eye to eye with the author in this method of imparting instruction, it is clear that it is a book that the student wants and will have.

Normal Bones and Joints Roentgenologically Considered. By ISIDORE COHN, M.D., F.A.C.S. Pp. 218 + xxxii, with 251 illusts. 1924. New York: Paul B. Hoeber. $10.

THIS is the fourth volume of a series published as the *Annals of Roentgenology* under the editorship of James T. Case, M.D. It opens with a foreword by Rudolph Matas, which describes in a most interesting manner the growth of our knowledge of bones in their structure and development which has sprung from Roentgen's discovery of 1895. The work itself is admirable in its simplicity and clearness. For the most part it deals only with the normal bones at their articular extremities. There are six chapters devoted to the main joints of both upper and lower extremities. Each chapter begins with a series of extracts from standard works on anatomy and surgery, giving the current views about the development of the epiphyses. Then follow excellently reproduced X-rays of the joint in question, taken at various ages from infancy up to adult life. These are of the utmost value in giving definite evidence about the centres of ossification and their dates of fusion, and also in providing reference plates with which any given clinical condition may be compared. Only in connection with the elbow-joint is any detailed reference made to traumatic conditions. We would suggest that it would be of the utmost value if typical injuries were figured of all the regions described, and also if the varying normal conditions of the shafts of the bones, as well as their extremities, were given at different periods of life, especially those of old age. The book will be an invaluable work of reference.

Diagnostic et Traitement des Maladies de la Vésicule biliaire par l'Excrétion vésiculaire provoquée. By M. CHIRAY and M. MILOCHEVITCH, Paris. Crown 8vo. Pp. 156, with 13 illustrations. 1924. Paris: Masson et Cie. Fr. 12.

A NUMBER of tests have been devised whereby a flow of bile is excited and the resulting fluid collected through a duodenal tube. In this book the theoretical basis and the practical application of such tests are discussed. Stimulation of the duodenal mucosa by 30 per cent magnesium sulphate (Meltzer-Lyon test) is the method most under consideration, but the use of 5 to 10 per cent peptone (Stepp's test) and sulphuric ether (Katsch test) is also reported on.

The authors have dealt systematically with the subject in its different aspects. A full account of the technique of passing a duodenal tube is given, together with the means by which the stages of its progress to its final site may be observed and verified. The difficulties that may arise, both in passing the tube and in obtaining pure samples of the fractions of bile, are indicated. A section of the book is devoted to the hypotheses concerning the derivation of the fractions of bile, more especially the second, which is considered by some to come from the gall-bladder and by others to be an increased flow direct from the liver. Further sections deal with the diagnostic value and the therapeutic value of the tests. The book concludes with a résumé of the more recent work on the subject.

La Transfusion du Sang. By P. EMIL WEIL and PAUL ISCH-WALL. Pp. 248, with 18 illustrations. 1925. Paris: Masson et Cie. Fr. 20.

THIS work constitutes a complete monograph on the subject of blood transfusion, and though there is little in it which has not already been written by other authors, the book is one which we can thoroughly recommend to the profession. It is essentially a practical treatise, and though theoretical considerations are, here and there, introduced, they do not bulk so largely as to confuse the reader and distract his attention from the proved therapeutic value of blood transfusion.

The authors insist on the simplicity of the operation, and also the safety of its employment when the bloods have been found to be compatible, and urge its extended use, especially at an earlier stage, in whatever condition it is indicated. With this view we entirely agree, as, with the authors, we feel sure that the fancied difficulties of technique, the supposed dangers arising from mixing the bloods of different people, and the poor results so often attained with blood transfusion from using it as a last resource, are responsible for the tardy acceptance of this essentially physiological method of treating many surgical and medical complaints.

The authors state that all the indications are not as yet definitely fixed; however, accumulated experience permits them to say that imperative indications are hæmorrhages of all kinds, shock, and anæmic states. In many other conditions beneficial results will be attained, though good will not always follow, especially if only employed late in the disease, viz., puerperal infections, pre-operative and post-operative therapy, pernicious and other forms of anæmia, etc.

There are ten chapters, headed as follows: Historical; Biology of transfusion; Citrated blood; Accidents; Methods of preventing accidents; Technique; Surgical indications; Obstetrical indications; Medical indications; Transfusion of blood in the infections; Conclusions. The book is terminated by a comprehensive bibliography, which is arranged in such a way that there can be no difficulty in finding the desired reference, as it is also tabulated under the same headings as the chapters in the book.

Les Hépatites dysentériques et leur Traitement. By A. VALASSOPOULO and PAVLOS PETRIDIS. With a Preface by Dr. E. RIST. Royal 8vo. Pp. 145 + viii, illustrated. 1924. Paris: Masson et Cie. Fr. 12.

THIS book is based on experience gained in the Greek Hospital at Alexandria, and should be of interest to all called upon to deal with this disease. It is divided into two portions. The first deals fully with pathology, symptomatology, and medical treatment. Treatment by emetine is discussed very fully. In the surgical portion, written by Pavlos Petridis, although other methods are discussed, pride of place is given to the operation introduced by his father, Aristide Petridis, which is fully described and illustrated. This is one of those books written as the result of personal experience that are always instructive.

Traitement chirurgical de la Dilatation bronchique. By P. GUIBAL, Paris. Demy 8vo. Pp. 173, with 31 illustrations. 1924. Paris: Masson et Cie. Fr. 10.

THIS small book actually may be taken as an abstract of the various methods of surgical treatment of bronchiectasis, and as such is most excellent. After a brief review of the clinical forms of bronchiectasis and the anatomical relations, the rest of the book is devoted to the subject of treatment. The major portion is connected with thoracoplasty and removal of one or more lobes of lung.

Die Hyperostosen des Schädels. By DR. INASABURO NAITO, with Introduction by PROFESSOR SCHÜLLER. Imperial 8vo. Pp. 95, with 84 X-ray photographs and 2 plates. 1924. Vienna: Julius Springer. 3.25 dollars.

THIS short monograph gives a clear and well-illustrated account of the various conditions in which local or diffuse thickening of the skull bones occurs. The conditions described include rickets, acromegaly, Paget's disease, leontiasis ossea, ostitis fibrosa, exostoses, neoplasms, inflammatory thickenings including syphilis, together with traumatic and compensatory enlargements of the skull bones. Each group of cases is illustrated by a number of typical specimens, the structure and X-ray appearances of which are given in detail. This makes the book a very valuable work of reference. A short concluding chapter deals with the classification and differential diagnosis of these various conditions.

The Medical Year Book and Classified Directory, 1925. Edited by CHARLES R. HEWITT. Pp. 596. London: William Heinemann. 12s. 6d.

THIS is the second year of issue of this small guide to the medical profession in England, Scotland, and Wales. It gives a short account of the various medical authorities in this country, together with the Universities and teaching hospitals and their staffs. No doubt it will be useful as a book of reference, but its utility will be greatly enhanced if many inaccuracies are corrected. (For example, the external examiners at Birmingham and Bristol are put down as the Professors of Surgery.) The alphabetical list of consultants and specialists is an original feature and may serve a useful purpose.